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EXPERIMENTAL NON-PARALYTIC POLIOMYELITIS: FREQUENCY, AND RANGE OF PATHOLOGICAL INVOLVEMENT[1]

DAVID BODIAN AND HOWARD A. HOWE

Poliomyelitis Research Center, Department of Epidemiology, Johns Hopkins University

Variation in degree of pathological involvement of the brain and spinal cord is a well known characteristic of paralytic poliomyelitis. An even greater variation in this respect was shown to occur in non-paralytic poliomyelitis in experimental animals (Bodian and Howe, '41; Howe and Bodian, '42). It was then found that in such infections of rhesus monkeys almost every degree of severity and spread of pathological change could occur, from isolated involvement of the olfactory bulbs after intranasal inoculation to the full-blown pathological picture usually seen in paralytic cases in the brain and spinal cord. Absence of paralysis was due not only to absence of lesions in the spinal cord but also at times to the fact that moderately severe lesions in the cord were so scattered that no muscle or muscle group was weakened to a clinically appreciable degree (also Kling, Olin, Magnusson, and Gard, '39; and Sabin and Ward, '41).

Our enlarging experience with rhesus monkeys has not only made possible a more extended documentation of earlier findings, but has also given evidence concerning the approximate frequency of non-paralytic and inapparent infections, and has indicated that such infections may occur about as often after inoculation by the intracerebral route as by peripheral portals. Although until recently all of our non-paralytic infections in rhesus monkeys have been induced by inoculation of fresh human material into peripheral portals,[2] it did not seem unlikely that they could also occur following intracerebral inoculations, especially when low titer inocula were used (Sabin and Ward, '41). For this reason a series of 37 monkeys inoculated intracerebrally with material from throat swabs of poliomyelitic patients were examined histopathologically to make certain that non-paralytic poliomyeli-

[1] Aided by a grant from The National Foundation for Infantile Paralysis, Inc.

[2] 5 cases intranasal human stool; 7 cases intranasal chimpanzee stool; 1 case intracutaneous cord suspension, Wallingford strain (Trask and Paul, '36); 1 case intranasal cord suspension, Lansing strain.

tis was not missed, as well as to confirm the clinical diagnosis of poliomyelitis in the paralytic monkeys. The general analysis of the throat swab assays has been made elsewhere (Howe, Wenner, Bodian, and Maxcy, '44; Howe, Bodian and Wenner, '44). The purpose of this report is to present a comprehensive survey of the pathological findings in a large and homogeneous series of monkeys inoculated intracerebrally with small amounts of presumably low titer human material, and to summarize our entire experience with non-paralytic infections in rhesus monkeys.

FREQUENCY OF NON-PARALYTIC INFECTIONS

It was a matter of some interest to find that the frequency of non-paralytic infections in our intracerebral series was about the same as that of non-paralytic infections in animals inoculated intranasally with human stools. Thus, of all rhesus monkeys inoculated intranasally with human stool suspensions from single cases, 45 have suffered paralysis, and there have been 5 non-paralytic infections, diagnosed histopathologically. A comparable frequency was found in rhesus monkeys used to assay chimpanzee stools for virus by intranasal inoculation. Of 50 positives in our total experience, 43 were paralyzed and 7 suffered non-paralytic infection. In our series of intrathalamic inoculations with material from human throat swabs obtained from single cases (total of 37), there have been 9 paralytic monkeys, and one which suffered a non-paralytic infection. These results leave no doubt that a histopathological examination of monkeys inoculated with low titer virus, and which do not develop paralysis, is of considerable value, since the positives can thereby be increased by approximately 10%.

It cannot be assumed, however, that this ratio of paralytic to non-paralytic infections in rhesus monkeys is necessarily similar to that which occurs in other species of experimental animals or in natural infections in man. Our chimpanzee experience, for example, suggests that a higher proportion of non-paralytic infections occurs in this species, especially when the alimentary tract has been used as the portal of inoculation. This experience will be presented in detail in a separate report.

RANGE OF PATHOLOGICAL INVOLVEMENT

After intranasal inoculation the existence of non-paralytic infection can be determined by examination of serial sections of the olfactory bulbs alone (Bodian and Howe, '41). Animals are killed one month after inoculation. For animals inoculated by other routes serial sections of blocks taken from the medulla oblongata in the region of the fourth ventricle, and from the cervical and lumbar enlargements of the spinal cord are examined. Single blocks about 7 mm. long from each of these regions are adequate ordinarily, but in rare instances lesions may be scattered or absent in the regions chosen, and additional blocks must be cut to establish the diagnosis. It is our custom to section additional cord blocks and the entire brain in certain doubtful instances, since a diagnosis of poliomyelitis can be made with certainty when the characteristic distribution of lesions is found in brain centers (Bodian and Howe, '40). In some instances, however, lesions consisting of focal and perivascular lymphocytic infiltrations may be few in number in the brain and of much greater intensity in localized segments of the cord, accompanied by evidence of neuronophagia in the latter regions.

Findings in Positive Cases. All of the monkeys which became paralyzed after intracerebral inoculation with material from human pharyngeal swabs showed typical infiltrative and neuronal lesions in the spinal cord, of moderate to severe intensity, and a characteristic distribution of lesions in the brain. The one case of non-paralytic infection (A789) showed a histopathological picture quite similar to that seen in the paralytic monkeys (Table I, Plates 1 and 2). Absence of paralysis was due only to the scattered distribution of the lesions in the cord, as explained elsewhere (Sabin and Ward, '41; Bodian and Howe, '41). A comparison of this type of non-paralytic infection with others which have occurred in our experience is instructive. Table I shows the distribution of lesions in the cerebrospinal axis from the olfactory bulbs to the spinal cord, in centers most commonly involved in poliomyelitis. As is seen in this table, the distribution of lesions along the cerebrospinal axis may vary exceedingly, both in monkeys with, as well as in those without, paralysis. In monkeys which developed paralysis after intracerebral or intranasal inoculation, as seen in the examples

TABLE I

Distribution of Lesions in Nervous Tissues of Rhesus Monkeys

	PARALYTIC CASES				NON-PARALYTIC CASES												
	Portal of inoculation				Portal of inoculation												
	Cerebral		Nasal		Cerebral	Cutaneous	Nasal										
	592	A819	A14	A692	A789	866	A172	A254	A503	A331	A89	A252	A704†	A169‡	A118‡	A835	A146	A804
Brain																	
Olfactory bulbs	—	—	cccc****	ccc***	—	—	cc***	cc***	c**	c**	cc***	cc**	ccc***	cc***	cc**	cc***	c**	**
Secondary olf. centers	—	—	cc**	c	—	—	c*	cc*	c	c	cc**	c	cc	c*	c	—	—	—
Preoptic area & hypothal.	cc**	c*	c**	—	cc**	—	c*	cc**	c*	cc	cc**	c*	cc**	c*	c	—	—	—
Globus pallidus	cc***	—	cc**	—	c**	—	—	c*	c*	*	—	—	—	c	—	—	—	—
Hippocampus	—	—	—	—	ccc**	—	—	—	—	—	—	—	—	—	—	—	—	—
Motor cortex	cc***	—	cc***	—	cc**	*	c*	cc*	c*	cc*	cc	—	c*	—	—	—	—	—
Lateral thalamus	cc***	c	cc**	c	c**	—	c	c*	c*	cc*	c*	c*	c	—	—	—	—	—
Subthalamus & midbrain	cc***	c*	ccc***	—	cc**	c**	cc**	cc**	c*	c*	—	—	c*	—	—	—	—	—
III nuclei	**	—	c*	—	cc**	*	—	c	—	*	c	c	—	—	—	—	—	—
Cerebellar cortex	c*	—	c*	—	c*	—	—	—	c*	c*	—	—	—	—	—	—	—	—
Nuclei fastigii	c***	*	cc**	—	c**	*	c**	c*	c*	c*	—	—	—	—	—	—	—	—
Reticular formation	cc***	c*	ccc***	—	cc**	c***	cc*	cc**	c*	c	c	—	—	—	—	—	—	—
V nucleus (motor)	c**	—	*	—	c*	—	—	—	—	—	—	—	—	—	—	—	—	—
V nucleus (sensory)	c*	—	—	—	c*	—	—	—	—	—	—	—	—	—	—	—	—	—
VII nucleus (motor)	c***	—	c*	—	—	**	c	c	c*	c	—	—	—	—	—	—	—	—
Vestibular nuclei	cc***	*	cc****	—	c*	*	c**	cc**	c*	cc**	—	—	—	—	—	—	—	—
IX, X nuclei (sensory)	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
X nucleus (motor)	*	—	—	—	—	—	—	—	—	—	c*	—	—	—	—	—	—	—
XII nucleus	cc***	*	c***	—	—	—	—	c	—	c	—	—	—	—	—	—	—	—
Spinal Cord																	
Cervical	+	+	+	+	+	+	+	+	+	+	—	—	—	—	—	—	—	—
Lumbar	+	+	+	+	+	+	+	+	+	—	—	—	—	—	—	—	—	—

c = Perivascular cuffing.
* = Focal infiltrative lesions or neuronophagia.
\+ = Typical poliomyelitis lesions in spinal cord.
— = No lesions found.
† = Lesions in left olfactory bulb and in left side of brain only.
‡ = Lesions predominantly in right olfactory bulb, and in right side of brain.

shown in the first four columns of Table I, extensive and severe pathological reaction may be found in the brain as well as in the spinal cord (Columns 1 and 3), or the cerebral involvement may be quite light (Columns 2 and 4). Rhesus A692 is especially striking in showing minimal cerebral pathological reaction (Table I). In either event the lesions are restricted to certain centers of the brain in a pattern previously shown to be characteristic of this disease (Bodian and Howe, '40). The intranasal cases are readily distinguished from those inoculated intracerebrally by the presence of lesions in olfactory bulbs and secondary olfactory centers. It is remarkable that in the monkey which showed no paralysis after intracerebral inoculation (A789, column 5) the lesions in the brain are more extensive and numerous than in some monkeys which did develop paralysis (A819 and A692), and in which cerebral lesions are few in number, and absent in some centers where lesions are ordinarily found. To the fact that absence of paralysis does not necessarily mean absence of spinal cord lesions one may now add the fact that the cerebral lesions in paralyzed monkeys may be much less severe and extensive than in certain monkeys which show no paralysis.

The remaining non-paralytic cases shown in Table I illustrate in greater detail our earlier finding that arrest of downward spread of the pathological process may occur at any point in the cerebrospinal axis after intranasal inoculation. The first four intranasal non-paralytic cases (A172, A254, A503, A531) shown in the table exhibit the full-blown distribution of lesions from olfactory bulbs to spinal cord. A distribution such as this is seen in paralytic cases. The last three cases in the table (A835, A146, A804) had typical lesions only in the olfactory bulbs. The intermediate cases were found to have varying degrees of extension of pathological reaction down the brain stem from the olfactory bulbs, but no lesions in the spinal cord.

This series of cases may be summarized by the statement that the distribution as well as the severity of the cerebrospinal pathological involvement in poliomyelitis in rhesus monkeys varies widely within the limits imposed by naturally refractory centers. Lesions may be limited to the region of the portal of entry, or may be found throughout all the susceptible nerve centers, or may be intermediate in extent of distribution. If the extent of pathological reaction is a factor in de-

= = = = Typical poliomyelitis lesions in spinal cord.
— | — No lesions found.
= = = = Lesions in left olfactory bulb and in left side of brain only.
↑ ↑ ↑ ↑ Lesions predominantly in right olfactory bulb, and in right side of brain.

termining the degree of subsequent resistance to reinoculation, it must be supposed that considerable quantitative differences in such resistance are to be expected following non-paralytic as well as paralytic infections. It is of interest to compare our cases of non-paralytic poliomyelitis in rhesus monkeys to the four cases of non-paralytic poliomyelitis in cynomolgus monkeys (Macaca irus) described by Faber, Silverberg, and Dong ('43). These workers similarly found variability in degree of severity of lesions, but attributed the arrest of the downward progression of the pathological process from the site of intracerebral inoculation to previous repeated exposures of mucous surfaces to virus, with resulting partial refractoriness. Since our series of monkeys showing non-paralytic poliomyelitis had no such exposures to virus, but frequently exhibited the phenomenon of early arrest after intranasal inoculation, one must wonder whether their monkeys also were exhibiting a refractoriness unrelated to specific antigenic immunity processes. This must especially be considered since the cynomolgus monkeys in question had been selected because they had resisted previous inoculations. Moreover, the lesions described in their cases might be attributable to any one of the many peripheral inoculations which preceded the final intracerebral inoculation, since chronic lesions of poliomyelitis may persist for many months after the acute infection has subsided (Warburg, '31).

Confirmation of axonal spread as a factor in the distribution of lesions in the brain. A remarkable feature of the histopathological picture in case A789 was the presence of numerous typical focal and perivascular lesions in the left hippocampus and adjacent subiculum (Plate II, fig. 1). This region is rarely involved in human cases or in paralytic experimental animals inoculated by various portals (Bodian and Howe, '40). Occasional lesions found in the hippocampus, however, have suggested that this center is not absolutely refractory to poliomyelitis virus action, as is for example the visual cortex (area 17), but is rarely involved because of relative inaccessibility with respect to axonal connections with centers usually invaded. This explanation for the sparing of centers which are not inherently refractory to virus has received evidence from other sources (Bodian and Howe, '40) but confirmation of this concept is perhaps most striking in case A789. An explanation for the lesions in the left hippocampus was readily found

in the fact that the inoculating needle had penetrated the left fornix in the transverse fissure before entering the left thalamus (Plate I, fig. 2). The needle did not extend deeper than the dorsal thalamus, and so had not anywhere touched the hippocampus. Since most of the inoculum was placed in the thalamus, only traces of virus from the inoculum could presumably have contaminated the fornix fibers along the needle track. The virus then must have passed back along the fornix to invade the hippocampus. Lesions were found only in the layers of the cornu Ammonis and in the subiculum, but not in the gyrus dentatus or the neighboring pyriform cortex. This indicates that virus passed in retrograde direction along axons of the fornix to invade their cells of origin in the cornu Ammonis (see also Bodian and Howe, '41a). The ipsilateral mamillary nuclei also contained lesions. The right inoculum had not impinged on the fornix, and no lesions were found in the hippocampus or mammillary body on this side (Plate II, fig. 2).

Findings in Negative Cases: Pathological Diagnostic Criteria. In addition to the ten monkeys inoculated with human throat swab material and which proved to be positive, 23 others were examined histologically, in the manner described above. Of these animals five had had fever of at least 1°F. about one week after inoculation. This is to be contrasted with the ten positive animals, eight of which had had fever of at least 1°F. during the first week after inoculation. In seven of the 23 negative instances examined, no lesions of any kind were observed in the brain or spinal cord. The other 16 monkeys presented pathological changes which were not sufficient to warrant a critical diagnosis of poliomyelitis or any other disease, but which require comment, since they have been at times interpreted as significant (Kling, '40). These changes consist of true perivascular infiltrations of mononuclear cells around occasional vessels in the pia mater of the brain and spinal cord (Plate III). In a few cases similar cuffed vessels were also found underlying the ependyma of the third and fourth ventricles (Plates III and IV), but in no other part of the parenchyma of the central nervous system. The subependymal cuffing is associated in these cases almost invariably with the penetration of the inoculum into one of the ventricles (Plate III, fig. 5). One then usually

finds a reaction of the ependyma and subependymal tissues, with epithelial debris present as far back as the fourth ventricle (Plate IV). Although Kling has interpreted such changes as characteristic of non-paralytic poliomyelitis, it is our belief that they represent a mild non-specific inflammatory reaction to the intracerebral inoculation, or to non-viral components of the inoculum. Hurst ('32) found, in this connection, that a definite meningitis was provoked by the intrathecal inoculation of sterile normal cord.

In monkeys inoculated by routes other than the intracerebral, perivascular infiltrations in the meninges as the sole pathological changes are rarely found in our experience, and are insignificant when present. In addition to these non-specific changes, it may be added, confusion may be caused by non-specific glial accumulations under the ependyma of the brain ventricles, and by the misinterpretation of clumps of leucocytes in the lumen of vessels as perivascular infiltration, as seems to have been the case in the figures published by Kling, Olin, Gard, and Norlin ('39, quoted from Kling, '40).

Cord passage was attempted in seven of the sixteen monkeys which presented meningeal perivascular infiltration and subependymal cuffing as the sole pathological findings in the brain and cord. 0.8 cc. of 20% suspension of lumbar and cervical cord enlargements was inoculated into the thalamus of two normal rhesus monkeys in each of the seven cases. None of the inoculated monkeys subsequently showed any signs of poliomyelitis. A similar experience has been reported by Sabin and Ward ('41), who failed to obtain virus from nervous tissues of monkeys exhibiting only meningeal and subependymal infiltrations.

In short, we feel that the pathological diagnosis of poliomyelitis can be made only by the finding of typical parenchymal lesions in the cord, including neuronal necrosis and neuronophagia, and focal and perivascular infiltrations, or by the finding of similar infiltrative lesions distributed in characteristic fashion in the brain, as previously described (Bodian and Howe, '40). Such findings are more reliable for diagnosis of non-paralytic infection than are clinical criteria, especially since many infections are clinically inapparent.

SUMMARY

1. Of 37 monkeys inoculated intracerebrally with material from pharyngeal swabs of poliomyelitis patients in Chicago and New Haven in 1943, ten suffered attacks of poliomyelitis. Of these, nine were paralyzed and one had a non-paralytic infection. The pathological findings in all cases were typical of poliomyelitis.

2. The occurrence of one non-paralytic infection in a total of 10 positive monkeys inoculated intracerebrally, is to be compared with a similar frequency of non-paralytic infections in monkeys inoculated intranasally with human and chimpanzee stools (human stools, 45 paralytic and 5 non-paralytic; chimpanzee stools, 43 paralytic and 7 non-paralytic).

3. Sixteen of the 23 negative animals examined histologically presented scattered perivascular infiltrations in the pia mater, which were interpreted as non-specific reactions to the inoculation. Cord passage to two normal rhesus monkeys in each of seven of these cases gave a negative result.

4. The range of pathological involvement in non-paralytic infections, as in paralytic cases, was found to be wide. The distribution, within the limits imposed by resistant centers, varied from arrest of the pathological process near the portal of entry to severe and extensive involvement of all susceptible centers along the cerebrospinal axis. It is suggested that this variability may be a factor in the degree of resistance to re-inoculation.

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PLATE 1

FIG. 1. Seventh lumbar spinal cord segment of rhesus A789, which suffered an attack of non-paralytic poliomyelitis. 15μ section stained with gallocyanin and showing characteristic perivascular and focal infiltrative lesions, and neuronophagia. Paralysis was absent because of the scattered nature of the spinal cord lesions. × 150.

FIG. 2. Section through left thalamic region of rhesus A789, showing the site of inoculation (i) in the thalamus, and passage of inoculating needle through the fornix (f). cc.—corpus callosum. 60μ, gallocyanin, × 20.

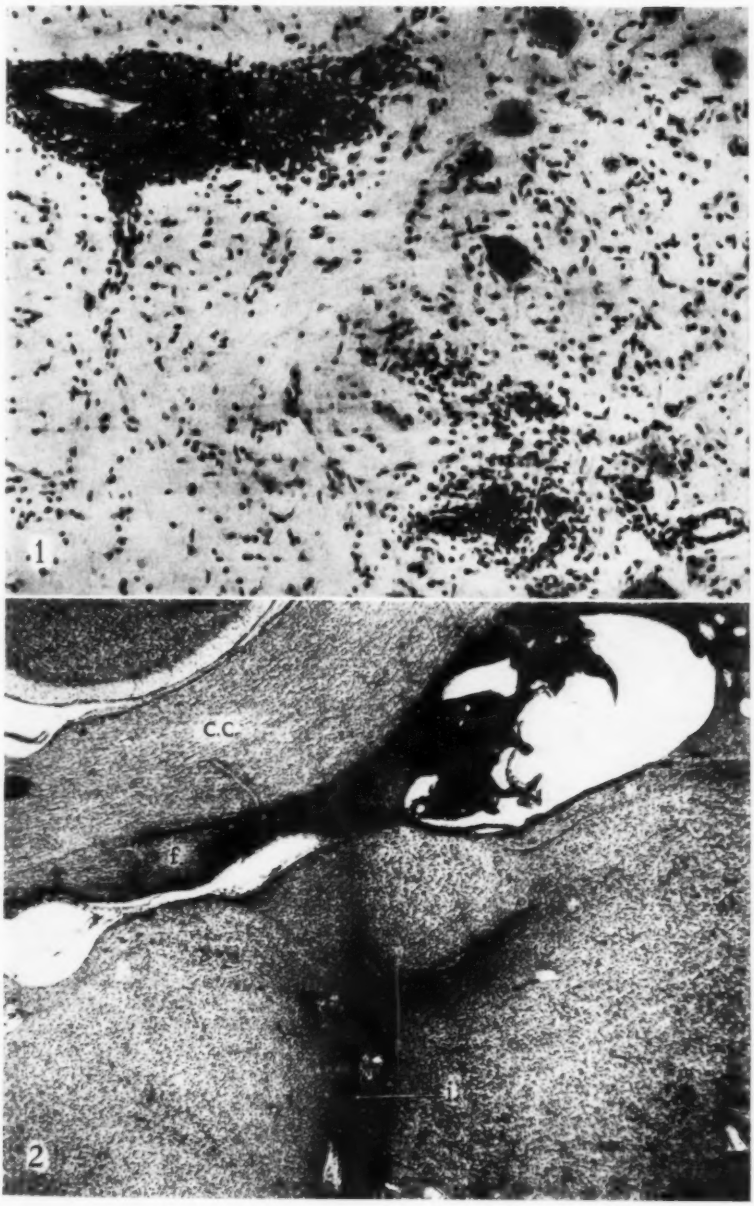

1
C.C.
f
2

PLATE 2

FIG. 3. Region of left hippocampus, rhesus A789, with arrows showing numerous perivascular and focal infiltrative lesions in cornu Ammonis (above) and in subiculum (below, left), 60μ, gallocyanin, $\times$ 20.

FIG. 4. Region of right hippocampus, rhesus A789, showing absence of lesions. 60μ, gallocyanin, $\times$ 20.

3

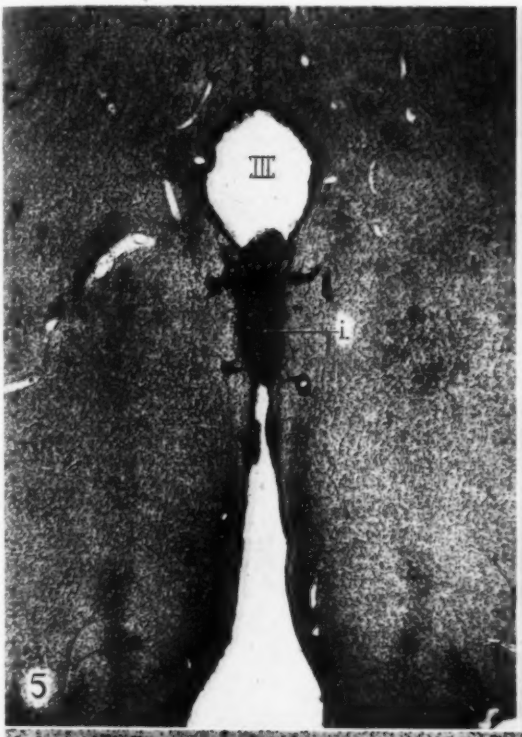
4

PLATE 3

FIG. 5. Rhesus A820, region of 3rd ventricle (III), showing accidental placing of inoculation (i) in the ventricle, with neighboring non-specific reaction of subependymal cuffing, resembling poliomyelitis cuffing. No lesions of this type were found in the remainder of the substance of the brain or spinal cord. 60μ, gallocyanin, $\times$ 20.

FIG. 6. Rhesus A820, showing perivascular cuffing (pv) in pia mater of medulla oblongata, probably due to non-specific reaction to inoculum escaping into spinal fluid. 60μ, gallocyanin, $\times$ 40.

FIG. 7. Rhesus A792, showing perivascular cuffing (pv) in pia mater of medulla oblongata, probably due to non-specific reaction to inoculum escaping into spinal fluid. No lesions were found in the substance of the brain or spinal cord. 60μ gallocyanin, $\times$ 40.



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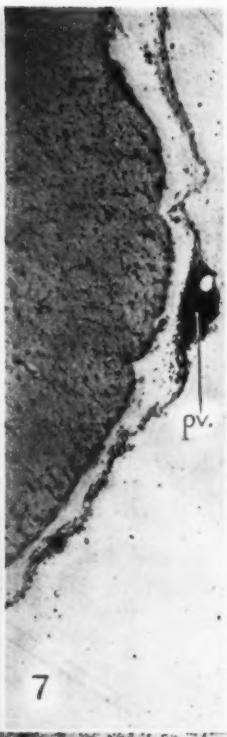

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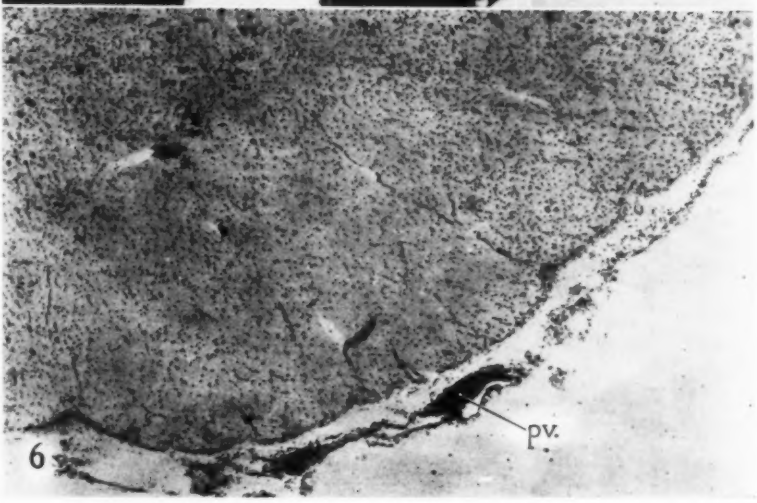

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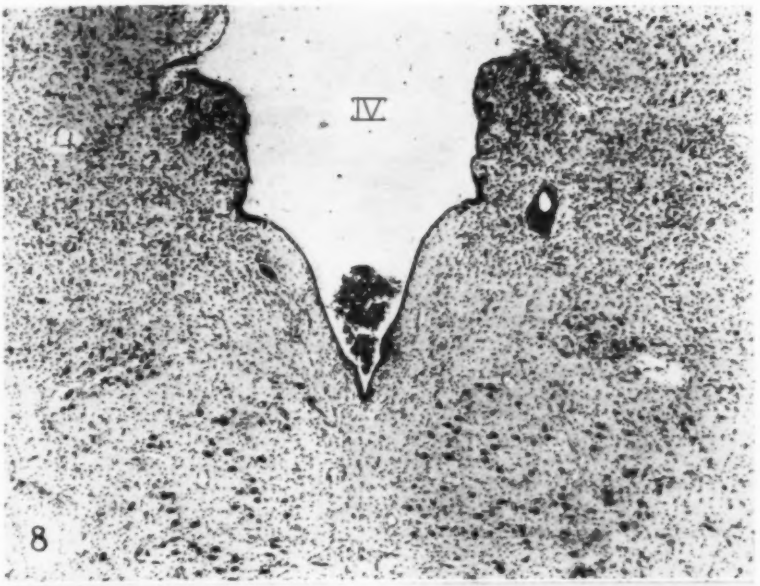
PLATE 4

FIG. 8. Rhesus A792, section through hypoglossal nucleus and 4th ventricle (IV). Note cellular debris in floor of ventricle, and neighboring subependymal perivascular reaction, mimicking that seen in poliomyelitis. No other lesions were found in the rest of the parenchyma of brain or spinal cord. 60μ, gallocyanin, $\times$ 40.

FIG. 9. Rhesus A849, showing reaction similar to that in fig. 8. 60μ, gallocyanin, $\times$ 40.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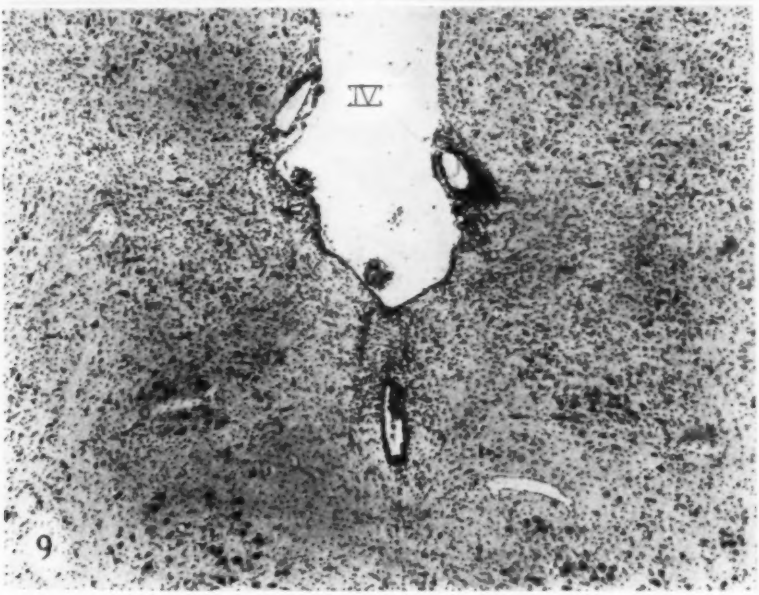
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FURTHER OBSERVATIONS ON THE PRESENCE OF POLIOMYELITIS VIRUS IN THE HUMAN ORO-PHARYNX[1]

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A recent paper (1) has reported the recovery of poliomyelitis virus from the oro-pharynx in 50% of a group of 14 poliomyelitis cases hospitalized in New Haven, Connecticut in 1943. The current communication extends the observations to a total of 20 cases in New Haven and 16 cases in Chicago, Illinois also studied during the late summer of 1943.

MATERIAL AND METHODS

The cases with 2 exceptions were diagnosed as poliomyelitis on the basis of the finding of fever, neck and back rigidity, increased numbers of leucocytes in the spinal fluid, with or without flaccid paralysis. All were hospitalized. Material was obtained by rubbing the oro-pharynx lightly with two $\frac{3}{4}''$ sterile cotton swabs which were then either moistened with distilled water or placed dry into small vials and frozen on CO_2 ice. Swabs were taken over periods varying from 1 to 9 days following the onset of the acute illness.

Tests were performed by eluting the material from the cotton in phosphate buffer at pH 8 since it had been previously shown (2) that this was the optimum hydrogen ion concentration for recovering Lansing virus from cotton swabs soaked with infected mouse cord emulsion. The eluate was then brought to pH 7 and treated with 20% ether in the ice box until sterile (18–36 hours) at which time the ether was removed. In no case was more than 1.1 cc. of inoculum obtained, which made it possible to give the entire specimen by intracerebral inoculation to a single monkey. Rhesus monkeys of 8–10 lb. were used. Under ether anaesthesia a trephine hole was made through the skull over the sagittal suture just posterior to the

[1] Aided by a grant from The National Foundation for Infantile Paralysis, Inc.

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coronal suture. It was thus possible through this single opening to place half of the inoculum into each lateral thalamus. This region was chosen because of its relatively high susceptibility and its deep position, which minimized regurgitation of the inoculum.

The criteria for successful isolation of virus were the production of flaccid paralysis with typical lesions in the spinal cords of the experimental animals, or the production of indubitable lesions alone (one case). Several instances were encountered in which animals showed no clinical signs of poliomyelitis but sections of the brain stem revealed light subependymal cuffing, usually in relation to some exudate in the 4th ventricle. These findings are discussed in the preceding communication. The animals were regarded as negative but to rule out atypical forms of response to virus, 7 different cord samples were passed intracerebrally into 2 monkeys for each. None produced any signs of disease.

In some instances test monkeys which showed no signs of having received infectious throat swab material were challenged by inoculation of active virus. Two of 5 animals remained well under these conditions but the interpretation of these findings is so obscure that these animals were regarded as negative.

ISOLATION OF VIRUS

In the entire series of 36 cases the number from which virus was recovered was 10, or 28%. This figure, however, without further analysis gives little idea of the factors actually involved. In the 20 New Haven cases virus was isolated from 8 (40%), while in the 16 cases comprising the Chicago series virus was found in only 2, or 12%. This disparity is clearly explained in tables I & II where it may be seen that in no instance was virus isolated after the 3rd day of the disease. The apparently unfavorable result in the Chicago series was occasioned by the fact that $\frac{2}{3}$ of the swabs were obtained between the 4th and 9th day of illness, whereas $\frac{2}{3}$ of the New Haven material was collected by the 3rd day. Thus in the New Haven group the majority of the cases were recent while the reverse was true of the Chicago patients. If the figures for virus recovery are based upon the number of cases assayed within the first three days of illness the disparity between the two groups largely disappears. Thus in 17

TABLE I

Poliomyelitis Virus in Human Throat Swabs

PATIENT	SERIES	AGE	TYPE	DAY OF DISEASE	EXPERIMENTAL ANIMAL			
					No.	Paralysis	Sections	Resistance to active virus
		yrs.						
Houde	N. Haven	6	NP	1	A816	+	+	
Hill	N. Haven	13	BP	1	A821	+	+	
Johnson	N. Haven	15	NP	2	A817	+	+	
W. Greene	Chicago	15	NP	2	A866	+	+	
Wells	Chicago	26	BP	2	A859	+	+	
Mari	N. Haven	10	NP	2	A791	+	+	
Stowe	N. Haven	11	SP	2	A789	−	+	
Broccoli	N. Haven	11	NP	2	A819	+	+	
Morgan	N. Haven	15	BP	2	A794	+	+	
Gordon	N. Haven	3	SP	3	A854	+	+	
Gronin	N. Haven	10	NP?	1	A820	−	−	
Doerer	N. Haven	13	NP?	1	A822	−	−	
Byrnes	N. Haven	2.5	NP	1	A851	−	−	
Noa	N. Haven	8	SP	1	A818	'	−	
Gajewski	N. Haven	12	NP	2	A823	−	−	
Levitz	N. Haven	15	SP	2	A852	−	−	
Tower	N. Haven	15	SP	2	A853	−	−	
Johnson	Chicago	15	SP	2	A860	−		−
Maffei	N. Haven	10	NP	2	A850	−	−	
Stone	N. Haven	6.5	SP	2–3	A815	−	−	
Curfman	Chicago	6	NP	3	A855	−		−
Riley	Chicago	12	SP	3	A792	−	−	
Keller	Chicago	8	SP	3?	A862	−		+
G. Greene	Chicago	8	NP	4	A865	−	−	
Volski	Chicago	6	SP	4	A861	−		+
Quinn	Chicago	11	BP	4	A844	−	−	
Mooney	Chicago	13	BP	4	A845	−	−	
Lanette	N. Haven	13	BP	4–5	A814	−	−	
Mixon	N. Haven	10	BP	5	A849	−	−	
Lesniack	Chicago	2	SP	5	A858	−	−	
Weseman	Chicago	1	SP	5	A863	−	−	
Shuman	N. Haven	15	BP	6	A790	−	−	
Kleinman	Chicago	2	NP	6	A857	−		+
Carter	Chicago	12	SP	6	A846	−	−	
Abrams	Chicago	21	SP	8	A856	−	−	
Zambole	Chicago	1	SP	9	A864	−	−	

NP = Non paralytic cases,
SP = Spinal paralytic cases,
BP = Bulbar paralytic cases.

cases of this type from New Haven 8, or 47%, were found to be harboring virus while 2 of the 6 Chicago patients (33%) were likewise positive. (43% for both groups combined.)

While virus was isolated in all of the bulbar paralytic cases during the first three days of illness and less frequently from the other types of cases (Table II) this does not necessarily mean that the bulbar case is a more frequent source of virus. This series is very small and these relationships might easily be seen in a different light by the accumulation of more data.

TABLE II

Virus Isolation from Different Clinical Types of Poliomyelitis

	1–3 DAYS AFTER ONSET			4–9 DAYS AFTER ONSET	
	Total	No. +	% +	Total	No. +
Bulbar	3	3	100	5	0
Paralytic	8	2	25	6	0
Non-paralytic	12	5	42	2	0
Totals	23	10	43	13	0

DISCUSSION

These experiments were undertaken in the belief that the method of nasopharyngeal washing was probably inadequate for demonstrating virus, and that improvement of the technique for assaying the virus content of the pharyngeal walls might produce results comparable to the higher recovery rates for fecal virus which have been achieved through certain technical improvements.

Vignec, Trask and Paul (3) summarized the literature up to 1938 and reported an overall recovery rate of 15% for virus from the pharynx during the first 5 days of disease. During the subsequent 4 days the recovery rates dropped to a figure indicating only the occasional isolation of virus. This rate was maintained through a period of at least several weeks. It now seems apparent that these figures are much too low. When an admittedly crude technique employing only 1 test animal for each sample is capable of demonstrating virus in 43% of the acute cases it seems very probable that

virus is in reality present much more frequently than the test indicates. It is perhaps noteworthy that during the past 5 years technical improvements have increased the positive isolations of fecal virus during the first 10 days of disease from about 30% to the neighborhood of 80 or 90%.

It seems too striking for mere coincidence that the period at which virus is no longer readily demonstrable in the pharynx should coincide so closely with the estimates of other observers relative to the end of the period of maximal infectiousness of the patient. Thus Casey (4) who tabulated 36 cases of single exposure which were followed by disease, found that in each instance this single contact took place at some time during a period ranging from 3 days prior to 3 days after the onset of symptoms in the original case. Aycock (5) studying similar material found in 16 of 17 cases following single exposure that this exposure "fell between the 4th day preceding and the 5th day following the onset of the primary" case. Other observations have been made regarding the presence of virus (6) or evidence for the infectivity of the patient (7) during the latter part of the incubation period. While our material unfortunately affords no information regarding the presence of virus during the prodromal phase of poliomyelitis it seems, as far as it goes, to corroborate to surprising degree these inferences regarding the decline of maximal infectivity obtained by an entirely different method of investigation.

SUMMARY

1. Poliomyelitis virus was demonstrated in pharyngeal swabs taken from patients ill with the disease in the spinal and bulbar paralytic, and non-paralytic forms.

2. Virus was found to be present in 43% of a series of 23 cases from whom swabs were taken during the first 3 days of illness.

3. In no instance was virus found after the 3rd day of illness. (13 cases)

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PERFORMANCE IN RELATION TO ENVIRONMENTAL TEMPERATURE[1]

Reactions of Normal Young Men to Hot, Humid (Simulated Jungle) Environment

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The present global conflict requires men to live, work and fight in extremes of climate to which most of them have not been previously exposed. In some regions climate alone, apart from endemic diseases, has caused casualties and reduced the efficiency of personnel. The physiologic effects of hot environments has been one of the aspects of a long-term study designed to determine the effects of stresses likely to be encountered by military personnel. Observations on the responses of man to heat and his adjustments to the increased thermal load are not new. Almost two centuries ago, military surgeons laid down rules governing health and activity in the tropics (1, 2). Contemporary observations have assumed several forms. Lifelong inhabitants of hot climates and recently transplanted white men have been compared with inhabitants of temperate regions in regard to various physiologic functions (3, 4, 5). Small groups or single investigators, studying themselves, have examined the effects of passing from temperate into hot climates (4, 6, 7, 8, 9). The effects of heat on workers (many of them colored natives) in hot occupations have been described (10, 11, 12, 13, 14). Hot rooms or hot baths have been used to study the changes induced by abrupt alterations in environmental temperature (9, 10, 15).

The responses of normal men to hot, dry (simulated desert) heat have been previously reported (16). The effects of hot, humid (simulated jungle) heat are considered in the present report. This study has had three pertinent features: 1) the subjects were young adult, white inhabitants of a temperate climate; 2) the hot environment was

[1] Released for publication by the War Department Manuscript Board which assumes no responsibility other than censorship for the contents of this article.

purposely severe, more so than usually found in nature but not exceeding conditions encountered in some industries; 3) the transition from one environment to the other was abrupt.

EXPERIMENTAL PROCEDURE AND METHODS

Environment. Available data on tropical climates come from weather stations in clearings, on plantations and in cities, usually on the sea coast. Here the conditions are not necessarily representative of the thick jungle where men now live and fight. The environmental conditions of this study were based on the worst recorded jungle climates.

During the day, 8 A.M. to 5 P.M., the climate in the "Hot Room" was as follows: dry bulb temperature, 90°F. to 91°F., with transient fluctuations to extremes of 89°F. and 93.5°F.; wet bulb temperature 89°F. to 91°F. with occasional extremes of 87°F. and 92°F.; relative humidity 94% to 96% with transient extremes of 100% to 88%. During the night, 6 P.M. to 7:00 A.M., the dry bulb temperature was usually 83°F. to 85°F. (extremes 78°F. to 87°F.) and the humidity 75% to 80% (extremes 60% to 85%). Approximately one hour was required to change from day to night environment. No additional radiant heat was supplied. Air movement was not measured but at no time did it exceed that created by the marching men. Except for a 10 minute "clean-up" in the morning and in the evening, men lived in the hot room day and night for periods varying from 8 days to 4 weeks.

These studies were carried out from early spring (March) to mid-autumn (November). Therefore, the change from control (cool) to hot, humid environment varied from extreme to moderate.

Experimental Subjects. Sixty-four healthy enlisted men between the ages of 19 and 33 years (average age 22 years) volunteered as subjects. All but six were between the ages of 19 and 24. They were of various bodily configurations, in differing states of physical fitness and came from all parts of the United States.

Clothing. In most of the experiments the men wore regulation Army jungle coveralls, shorts, socks and jungle boots. Occasionally summer khaki was substituted for the coverall. During special studies only cotton shorts, socks and shoes were worn.

Preliminary Training. For one to two weeks before entering the

humid heat, the men performed the same work which they were to do later in the hot room. This accustomed the men to the work and the experimental procedures and tended to produce a more uniform state of physical fitness in all men.

Activity in the Hot Environment. The men were divided into two groups. Group I, Resting. Nine (9) men rested in the hot room for 7 to 11 days before beginning work as in Group II. Group II, Walking. Fifty-five (55) men performed work of moderate severity and long duration, walking at standard army pace while carrying a 20 pound pack. A walk of $2\frac{1}{2}$ miles in 47 minutes constituted a work-period. Between successive work-periods, a rest of 13 minutes was given during which observations were made. Unless incapacitated, men walked two (2) consecutive periods in the morning and three (3) in the afternoon; $12\frac{1}{2}$ miles a day.

Food. Food consisted of the standard Army garrison ration. Except for the first day in the hot environment the men ate heartily. No record was kept of the type or amount of food eaten.

Water. Salt was added to all drinking water (final concentration 0.1%). All fluid drunk was measured and administered in one of the three ways; (a) as much as desired, whenever wanted, (b) 300 cc. at the beginning and 300 cc. in the middle of each work-period plus as much as desired at all other times, and (c) restricted either to 200 cc. or 150 cc. per hour during the working day (6 A.M. to 5 P.M.) and thereafter as much as desired. In most observations, water was permitted ad lib.

Observations. Continuous notes were made of the appearance of the men and of their symptoms during work. The heart rate and blood pressure were determined at the beginning and end of each work period with the subject first erect, then supine (three minutes in each position). Posture was changed passively by a tilt table, occasionally by voluntary movement of the subject. Immediately on finishing a work-period, and before getting on the tilt table, the heart rate was counted with the subjects marking time. The rectal temperature was determined immediately before and after each work-period. At the beginning and at the end of each work period, the subjects stripped, dried off the sweat and were carefully weighed (within 5 grams). The water intake and urine output during each work period and for each day (24 hours) were recorded.

RESULTS

The results are presented in a series of representative charts showing typical changes in heart rate, rectal temperature, blood pressure and weight (sweat) loss. These simple measurements do not define completely the complex process of acclimatization but serve as indices of that process. In the charts to be presented, these indices were consistent with the picture in the man as a whole.

COMPARISON OF ACCLIMATIZED AND UNACCLIMATIZED STATES

The unacclimatized man works with a rapid heart rate, a high rectal temperature and an unstable blood pressure (first day, Chart 1). With continued exposure and work, he accomplishes the same amount of work with progressively less increase in heart rate and rectal temperature and with less disturbance of the blood pressure until in the acclimatized state (eleventh day, Chart 1) these values approximate those following similar work in the control (cool) environment. The changes are rapid at first, then more gradual.

The cardiovascular instability of the unacclimatized state is brought out by the erect posture which induces tachycardia, a low systolic blood pressure and a narrow pulse pressure (Chart 1). Symptoms of cerebral ischemia and even syncope occur. These changes (both subjective and objective) are more marked after work than during rest. On returning to the supine position, the heart rate and blood pressure return to normal and the symptoms of cerebral ischemia promptly disappear. Postural hypotension after working on the first day in "jungle heat" is a common occurrence. In one experiment, six of the fifteen men were unable to stand because of severe postural hypotension accompanied by disabling symptoms or syncope. As acclimatization progresses, the postural circulatory instability diminishes and disappears. Acclimatized men stand erect without difficulty.

In the remainder of this report, the observations, charts and conclusions are for men in the *erect posture* unless otherwise indicated. This choice was made because the erect posture places an added strain on the circulation and may reveal disturbances not otherwise apparent.

The acclimatized man works in humid heat almost as easily as in the cool environment. The unacclimatized man working in the heat becomes dull and apathetic, performs his work poorly and often develops to varying degrees, and either singly or in combinations, the symptoms and signs of heat exhaustion. In this study, these symp-

toms and signs appeared in the following order of frequency: *Symptoms* (1) fatigue, (2) headache, (3) dizziness, especially when erect, (4) loss

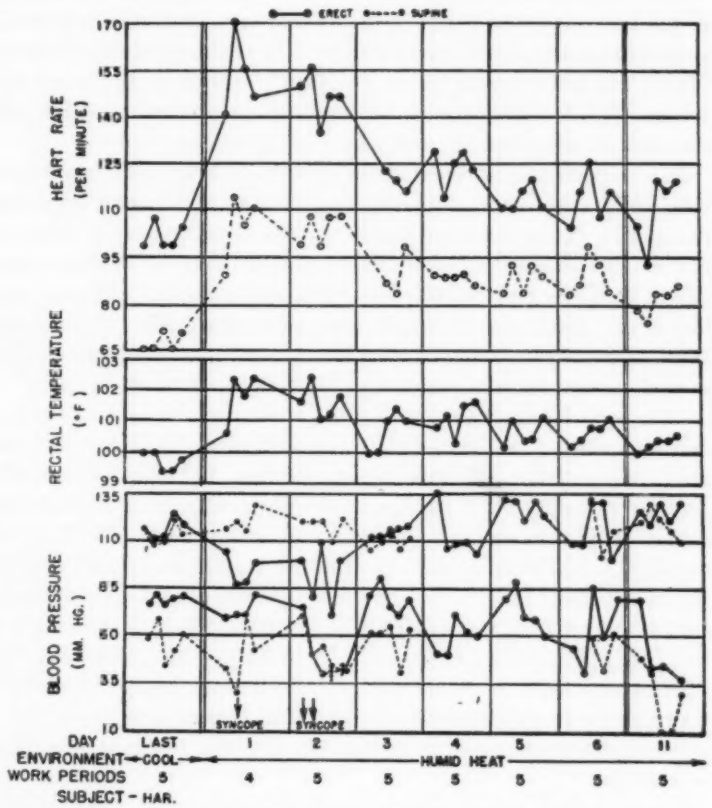

CHART 1. CHANGES IN HEART RATE, RECTAL TEMPERATURE AND BLOOD PRESSURE DURING ACCLIMATIZATION TO WORK IN HUMID HEAT. EFFECT OF CHANGE IN POSTURE

Each arrow above the abscissa indicates syncope in the erect posture

of appetite, (5) nausea, (6) abdominal distress, (7) vomiting and (8) shortness of breath. *Signs* (1) flushing of the face and neck, (2) rapid pulse rate (150–200/min.), (3) fever over 102°F., (4) lack of coor-

dinated effort (clumsy, stumbling), (5) staring, glazed eyes, (6) mental disturbances (apathy, poor judgment, irritability) and (7) collapse.

Most men when they first work in the heat develop a marked flushing of the face, neck and upper chest. There may be accompanying engorgement of the scleral vessels and swelling of the nasal mucous membranes, the latter giving rise to "sniffles." Edema of the hands also occurs. These manifestations of engorged peripheral vascular beds diminish or disappear as acclimatization develops.

It is important to stress that the changes in heart rate, blood pressure, and rectal temperature which accompany acclimatization do not necessarily define acclimatization nor do they invariably serve to differentiate the degrees of acclimatization attained by different men. Many variables not evaluated by such measurements influence performance. Each man should be considered as a whole and his symptoms, appearance, behavior and actual performance should receive careful consideration in evaluating his ability to work in the heat.

This point is illustrated by Chart 2, which indicates the changes in two men during acclimatization. In both men, the heart rate and rectal temperature fell with acclimatization, but the levels finally reached were different in the two men. Even when fully acclimatized, subject EIC. usually had a high rectal temperature (103°F.+) on completion of 5 work-periods, whereas the rectal temperature of SER. was much lower (100°F. to 100.4°F.). On the other hand, the heart rate of subject EIC. was relatively slow (100 to 115/min) while that of SER. was fast (125 to 140/min). At this time, both men were well acclimatized and completed the prescribed work easily. In neither man did the heart rate alone or the rectal temperature alone give a true concept of the capacity to perform or of the response to work in humid heat.

In most men, the heart rate and rectal temperature decrease proportionately during acclimatization. This is not always so and two different patterns of response have occurred in some acclimatized men: (1) high rectal temperature and slow heart rate (like EIC.) and (2) low rectal temperature and rapid heart rate (like SER.).

FACTORS IN ATTAINING AND MAINTAINING ACCLIMATIZATION TO HUMID HEAT

Course of Acclimatization. Acclimatization is initiated by the first exposure to heat, progresses rapidly during the first 3 to 4 days and then

more slowly to be complete in one to two weeks. This is illustrated by the observations on subject HAR. (Chart 1). On the first day this man was exhausted at the end of the 4th work period. The heart

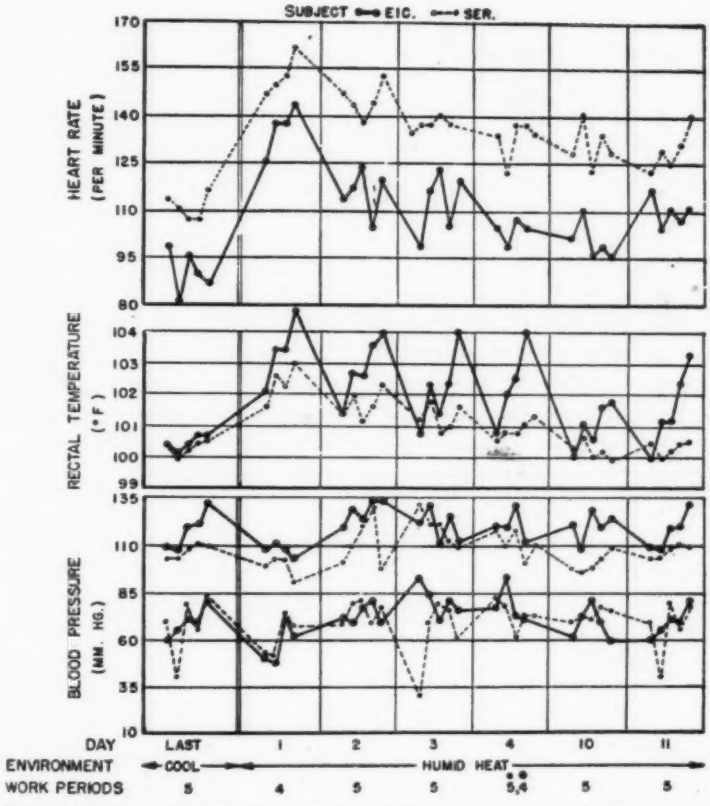

CHART 2. DIFFERENCES IN THE PATTERN OF RESPONSES OF THE HEART RATE AND RECTAL TEMPERATURE IN TWO TYPES OF MEN DURING ACCLIMATIZATION TO WORK IN HUMID HEAT

rate was rapid (147/min), the rectal temperature high (102.4°F.), and the blood pressure low (98/82 mm. Hg), with postural hypotension eventuating in syncope. On the second day he completed more work (5 periods) and with less discomfort, but marked physiologic disturb-

ances persisted. On the third day there was much improvement in all respects and this continued at a slower pace over the ensuing 8 days. At this time his response approximated, but did not equal,

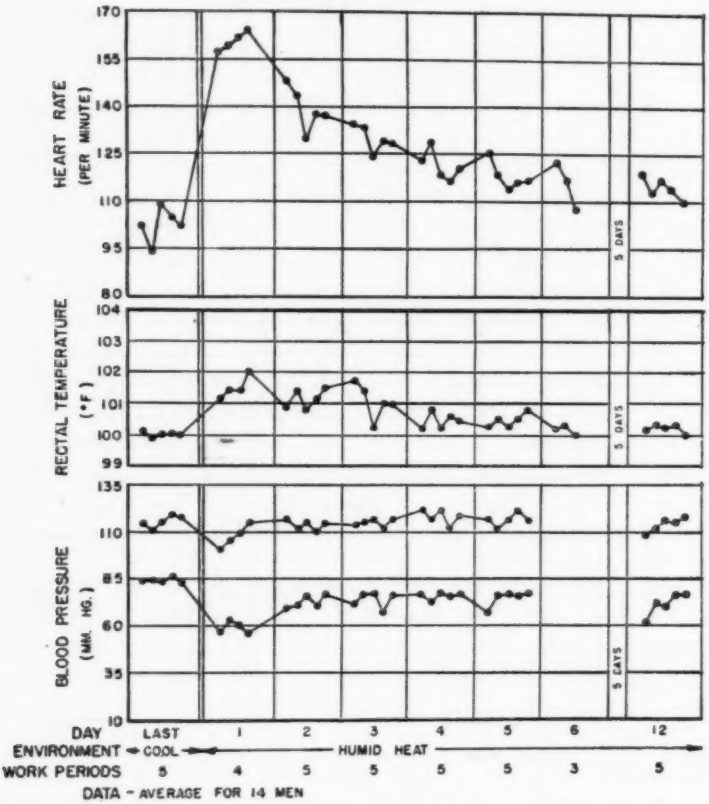

CHART 3. CHANGES IN HEART RATE, RECTAL TEMPERATURE AND BLOOD PRESSURE DURING ACCLIMATIZATION TO WORK IN HUMID HEAT

that observed in the control (cool) environment. Even in well acclimatized men the heart rate and rectal temperature usually remained slightly above that in the cool environment.

The typical pattern of acclimatization is emphasized by Chart 3, which is derived from the averaged data of 14 men.

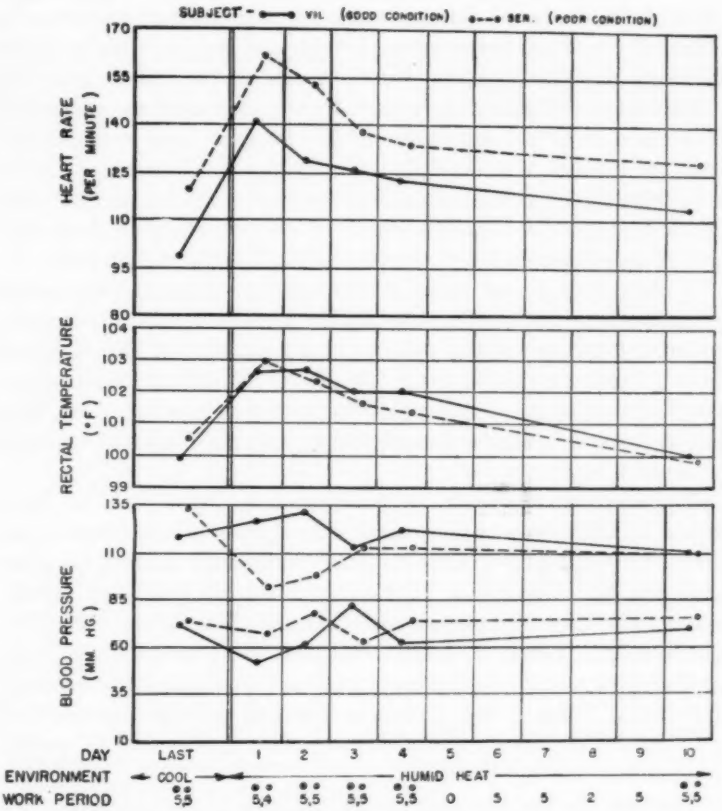

CHART 4. EFFECT OF PHYSICAL FITNESS ON THE COURSE OF ACCLIMATIZATION TO WORK IN HUMID HEAT

Physical Condition. Men in good physical condition generally acclimatize to heat more rapidly than men in poor condition and when acclimatized maintain the same relative superiority of performance in the heat that they did in the cool environment.

The course of acclimatization of a man in good physical condition (VIL.) is compared with that of a man in poor condition (SER.) in Chart 4. The differences between the two men are more apparent in their cardiovascular responses than in their thermal adjustments. Whereas the rectal temperatures of both men were essentially similar throughout acclimatization, the heart rate of the less fit man was always the more rapid and postural hypotension occurred on the first two days. The parallel course of the curves of heart rate indicates that the more fit man maintains the same degree of superiority in the heat that he did in the control environment. During the first days in the heat, the less fit man experienced more distress than the fit man but when acclimatized both men worked easily and energetically.

Activity Prior to and during Acclimatization. After the attainment of satisfactory physical fitness, further work in a cool environment seems not to improve the ability to work on the first day in humid heat. Resting for six (6) to ten (10) days in humid heat induces only a small degree of acclimatization. Acclimatization is achieved most rapidly by daily graded work undertaken simultaneously with exposure to humid heat.

The effect on subsequent acclimatization of (a) work in the heat, (b) rest in the heat and (c) continued work in a cool environment are compared in Chart 5. After the same preliminary training for three groups of men, one group (E) continued to work in the cool out-of-doors while the other two groups (C and D) entered the humid hot environment. Group D rested while Group C immediately began graded work which was continued until acclimatization was achieved (10 days). When Group C was acclimatized, all three groups were subjected on the same day (called comparison day in Chart 5) to five work periods in humid heat.

The men who had worked in the heat (Group C) worked easily, with low heart rates and rectal temperatures and normal blood pressures. In contrast, the men without previous exposure to heat (Group E) worked with difficulty, with rapid heart rates and high rectal temperatures. The men who had rested in humid heat (Group D) showed only a small degree of acclimatization, apparent chiefly in the improved temperature regulation, the less marked flushing and the fewer and milder symptoms. Resting in humid heat appeared to induce less

acclimatization for work in humid heat than the acclimatization for work in dry heat induced by resting in dry heat (120°F.). Appar-

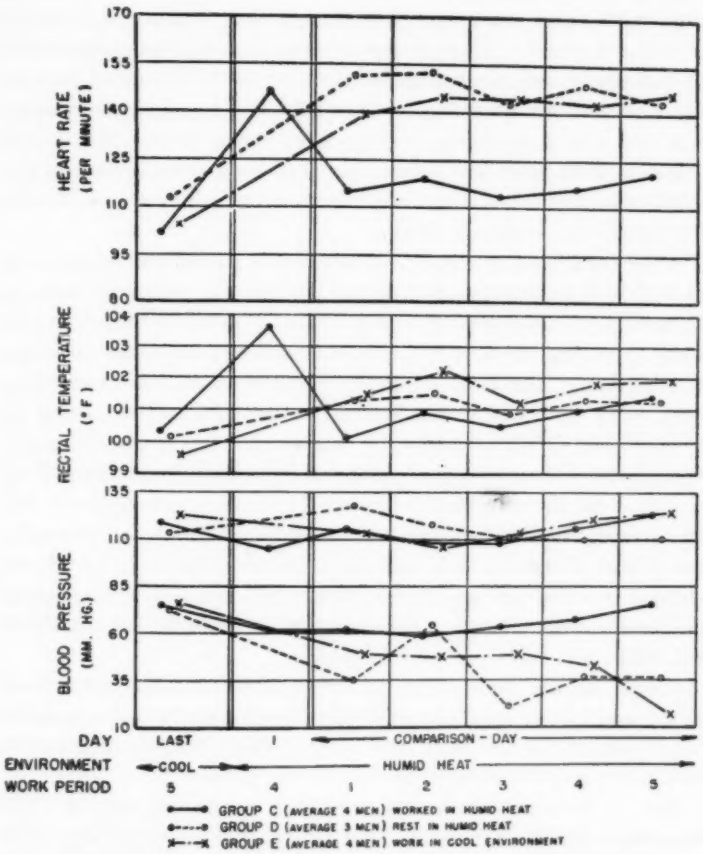

CHART 5. EFFECT OF PREVIOUS ENVIRONMENT AND ACTIVITY ON WORK-PERFORMANCE IN HUMID HEAT

ently the dry heat constituted a greater stress on the thermo-regulatory mechanisms of resting men than did the humid heat (90°F.).

Strenuous Work from First Exposure to Heat. Strenuous work on

first exposure to humid heat is not well tolerated. Fourteen (14) men were required to work for five periods on their first day in the humid heat. Only five men completed the task and they finished with difficulty, with rapid heart rates, high rectal temperatures and marked reduction in morale. Completing strenous work on first exposure does not necessarily indicate acclimatization, for the acclimatized man not only accomplishes strenuous work but does so easily, without symptoms and with a minimum of physiologic disturbance. Maintaining strenuous work from the outset may lead to a deterioration of performance in contrast to the steady improvement achieved on a schedule of progressively increased work.

Initial Intolerance to Heat. Intolerance to humid heat, even to the point of heat exhaustion, during the first days of exposure, does not decrease the acclimatization finally attained, *provided that* when such disability occurs, work is discontinued and rest, adequate water and salt are given. This is illustrated by the performance of two subjects whose early course in humid heat is plotted in Chart 6. From the outset subject GRO. worked with relative ease, few symptoms, a controlled heart rate and rectal temperature and a maintained blood pressure. On the other hand, subject COX. worked with great difficulty during the first two days, and complained of fatigue, headache, nausea and dizziness. His marked cardiovascular disturbance was indicated by the sustained tachycardia and the profound postural hypotension with syncope. Between work periods, he lay exhausted. Rest, water and salt were given liberally.

In spite of the poor early response, subject COX. acclimatized quickly and by the third day and thereafter his performance equalled that of subject GRO. Both men worked easily with well controlled heart rates, rectal temperatures and blood pressures.

Effect of Season (Previous Environment) on Acclimatization. The temperature at which men live prior to exposure influences the initial performance and the course of acclimatization to humid heat. The warmer the original environment, the better the initial performance and the more rapid the acclimatization.

Chart 7 indicates the amount of work performed by two groups of comparably fit men during their first six days in humid heat. The two groups entered the hot environment at different seasons of the year:

Group A (6 men) in mid-March; Group B (15 men) in early August. The "amount of work" performed by each group was taken as the total man-work-periods completed by the group divided by the total pos-

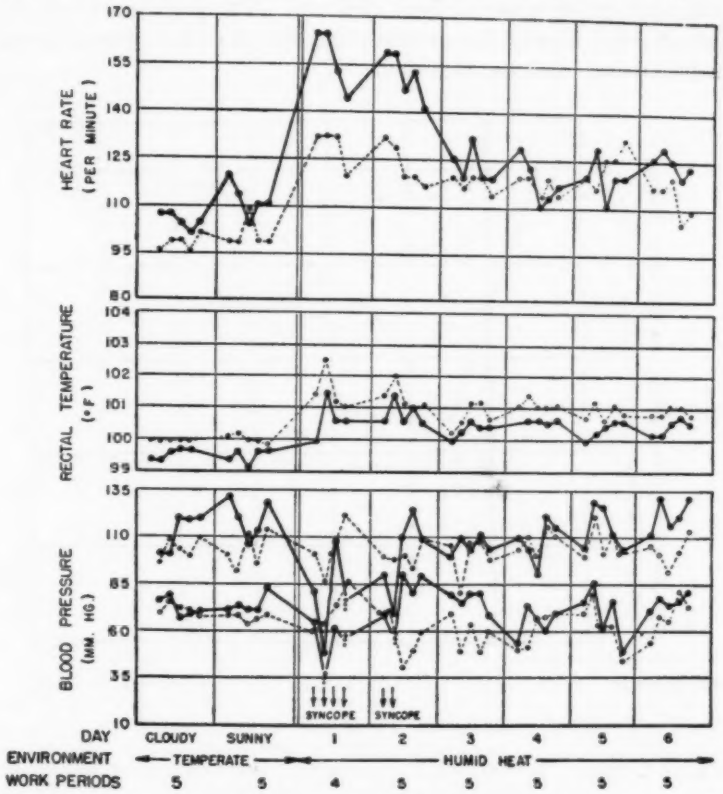

CHART 6. INTOLERANCE TO HEAT AND POOR WORK-PERFORMANCE ON THE FIRST DAY IN HUMID HEAT DO NOT ALTER THE RATE OR DEGREE OF FINAL ACCLIMATIZATION (GRO, SOLID LINE; COX, DOTTED LINE)

sible, i.e., 5× number of men in the group. The result was expressed as a percentage value. For example, if each of six men in a group completes only 4 periods, the amount of work done by the group is

$$\frac{6 \times 4}{5 \times 6} \times 100 = 80\%.$$

The mid-summer group (B) completed 80% of the prescribed work on the first day in humid heat, the mid-March group (A) only 46%. On the second day and thereafter, the August group completed the full work requirement without difficulty. The performance of the March group improved more slowly and the full work requirement was not achieved until the fifth day.

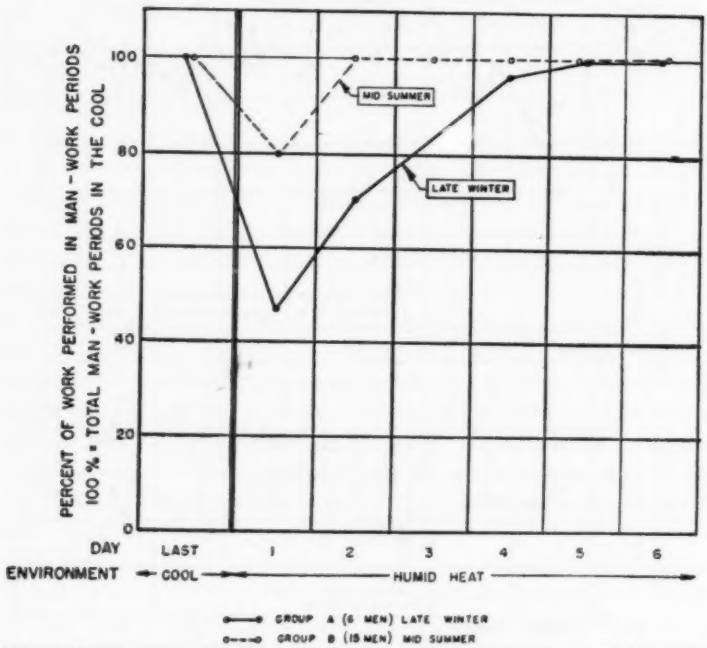

CHART 7. EFFECT OF PREVIOUS ENVIRONMENTAL TEMPERATURE ON AMOUNT OF WORK PERFORMED IN HUMID HEAT

Chart 8 indicates the averaged heart rate, rectal temperature and blood pressure of Groups A and B at the end of the last work period finished each day by the majority of men in the group. Although the March group (A) performed less work on the first days in humid heat than the August group (B), nevertheless, in doing that smaller amount of work Group A sustained greater subjective discomfort and more

marked physiologic disturbances (heart rates and rectal temperatures) than Group B. Postural hypotension with syncope on completion of work occurred in both groups.

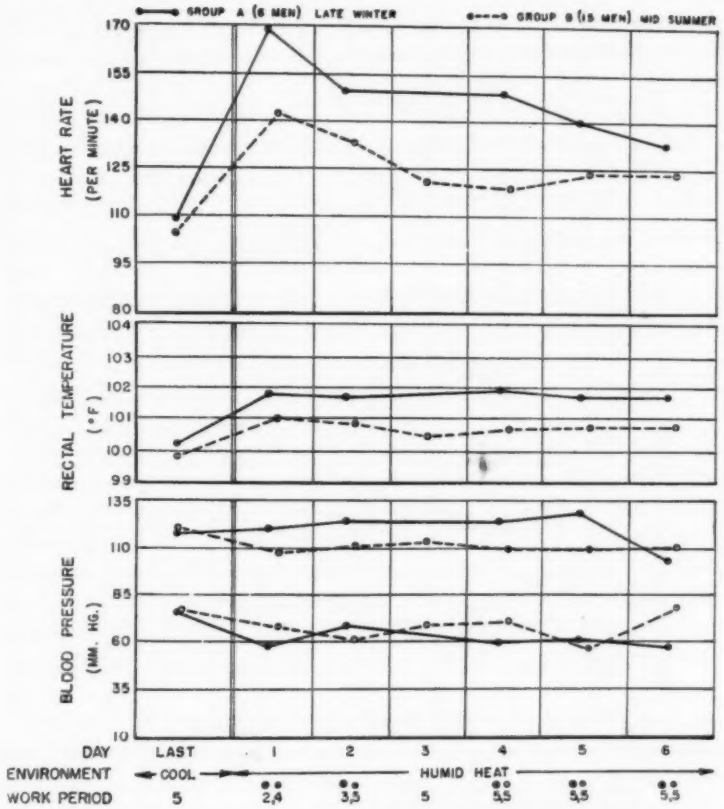

CHART 8. EFFECT OF PREVIOUS ENVIRONMENTAL TEMPERATURE ON ACCLIMATIZATION TO WORK IN HUMID HEAT

With continued work in humid heat, both groups improved subjectively and objectively. However, the improvement was slower in the March group (A) than in the August group (B).

Persistence of Acclimatization. After leaving the humid heat,

acclimatization is retained for varying periods depending on the climate into which the acclimatized men return. When this climate is

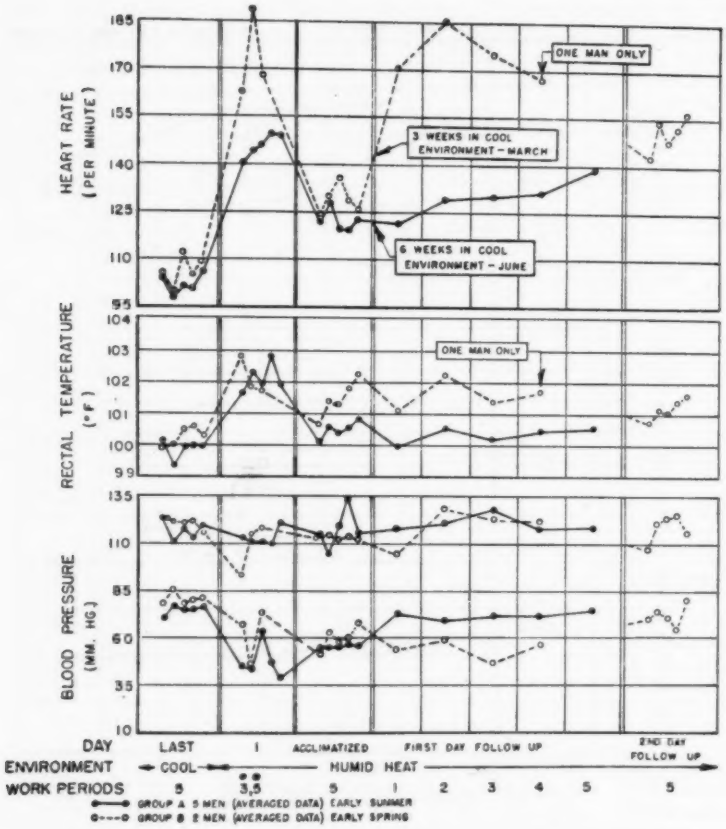

CHART 9. EFFECT OF SUBSEQUENT ENVIRONMENTAL TEMPERATURE ON PERSISTENCE OF ACCLIMATIZATION AFTER LEAVING HUMID HEAT

warm, acclimatization is retained for longer periods than when the climate is cold (Chart 9).

Two groups of men, one observed in May and June (Group A), the

other in March (Group B), were well acclimatized when they left the humid heat; Group A in late June, Group B in late March. After six (6) warm summer weeks, Group A returned in mid-July and worked in the humid heat; Group B returned in mid-April after 3 weeks in the cool early spring. Chart 9 shows that Group A still retained much of its acclimatization after six weeks, whereas Group B had lost most of its adaptation during an interval only one half as long. This was evident in the higher heart rates and rectal temperatures of Group B, in the fewer work periods completed (3 and 4 in contrast to 5) and in the apathetic, fatigued, flushed appearance of the men. The men in the summer group (A) stated that they worked as easily as six weeks previously when fully acclimatized. (Group B is small but similar results were obtained in other men.)

The March group (B) was re-exposed to the humid heat on the day after the first follow-up exposure. The performance was markedly improved in all respects (last column on right, Chart 9). The single re-exposure, though not well tolerated, had re-induced a considerable degree of acclimatization.

After the follow-up study in mid-April, the men in Group B returned to their regular duties. In late July, 3 months later, five men of this group again worked in the hot environment. Their performance was surprisingly good. In all respects, amount of work accomplished, subjective reactions and physiologic measurements, their performance was considerably better than at any other time except when fully acclimatized, and this they closely approached. Considerable acclimatization was apparently acquired during the warm summer months.

In all of these experiments, acclimatization was retained best by those men who had remained physically fit in the interval between exposures to humid heat.

Cross Acclimatization in Hot Dry and Hot Humid Environments. Acclimatization to dry (desert) heat induces a substantial degree of acclimatization to moist (jungle) heat (16). The reverse is also true but perhaps to a lesser degree.

Chart 10 indicates the averaged performance, on their first day in moist heat, of 3 men acclimatized to simulated desert heat (120°F. dry bulb temperature, relative humidity 18% to 22%) and of 6 men with-

out previous exposure to a hot environment. The desert acclimatized men had a far superior performance.

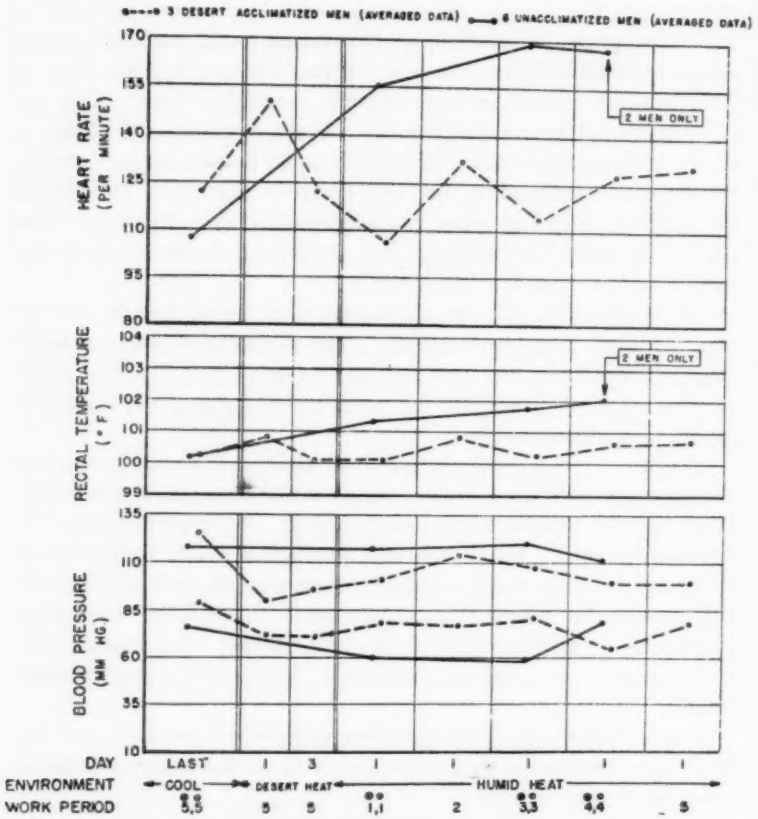

CHART 10. EFFECT OF PREVIOUS ACCLIMATIZATION TO DRY (DESERT) HEAT ON WORK-PERFORMANCE DURING FIRST EXPOSURE TO HUMID HEAT

Chart 11 indicates the averaged performance, on their first day in dry (desert) heat, of 4 men acclimatized to humid heat and of 5 men without previous heat exposure. Due to operational difficulties the environment on the test day was much too moist for a desert—dry

bulb temperature 120°F., relative humidity 26% to 29%. Nevertheless, the performance of the men acclimatized to moist heat was much the better. The men without previous exposure to heat did very

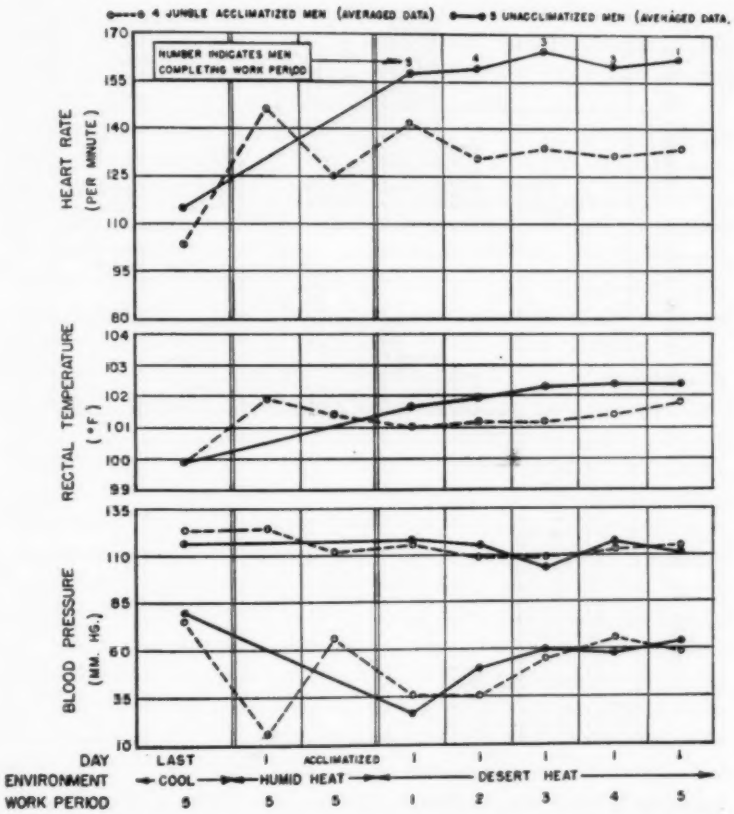

CHART 11. EFFECT OF PREVIOUS ACCLIMATIZATION TO HUMID (JUNGLE) HEAT ON WORK PERFORMANCE DURING FIRST EXPOSURE TO DRY (DESERT) HEAT

badly. Only one man completed the required five periods. All men were exhausted. Two had postural hypotension with syncope. All had elevated heart rates and rectal temperatures.

WATER BALANCE

Water Requirements. Work in hot, humid surroundings induces profuse sweating with the loss of large amounts of water and salt. The

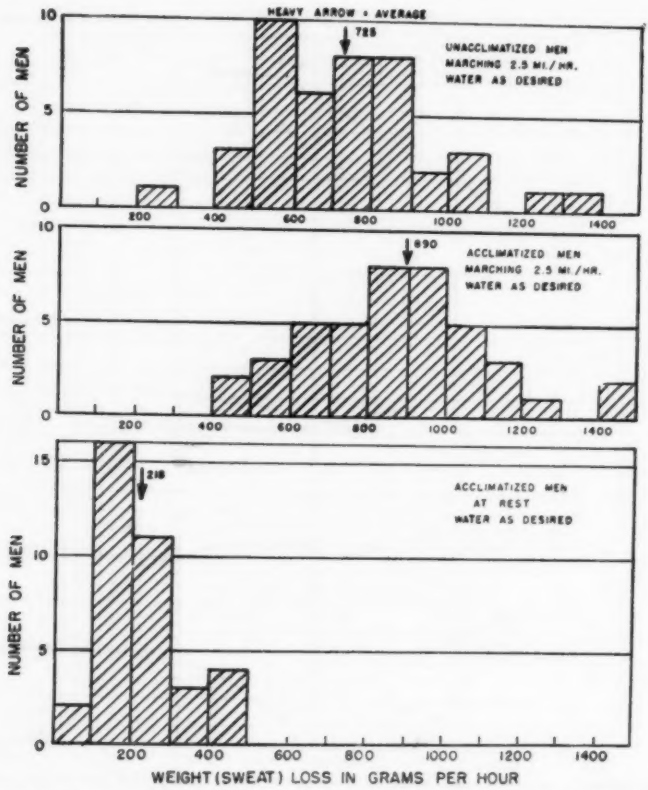

CHART 12. RATE OF WEIGHT (SWEAT) LOSS BY CLOTHED MEN DURING WORK AND REST IN HUMID HEAT

magnitude of the water losses, and therefore of the water requirement, was determined by measuring the weight (sweat) lost by men in performing prescribed tasks. Different men lose considerably different amounts of sweat during the same degree of activity. These variations are indicated by the histograms in Chart 12 in which the ordi-

nates (height of column) give the number of men who lost the amount of sweat per hour indicated by the class interval of the abscissa.

Resting men, lying on cots, lost an average of 218 grams per hour; range 77 grams to 480 grams. Unacclimatized men working on the first day in humid heat lost an average of 725 grams per work period; range 290 grams to 1310 grams. When acclimatized, the same men lost slightly more weight (sweat) per standard work period; average loss 890 grams; range 460 grams to 1405 grams.

These data apply only to clothed men in an environment where the dry bulb temperature is between 90°F. and 93°F., the wet bulb temperature between 88.5°F. and 91°F., and the relative humidity between 92% and 96%. The wide variation in weight (sweat) losses appears to result from several, as yet incompletely studied and understood, factors. Among these the effect of relatively small changes in environment is probably most important (Chart 19). Diurnal and seasonal (previous environment) influences also appear to be operative.

Water Drinking and Thirst. No man drank enough water voluntarily to replace the water lost in the sweat during work in humid heat (Chart 13). Thirst did not appear until considerable water deficits had developed. Since it lags behind the water needs, thirst constitutes an insensitive guide to the water requirement. When there is intolerance to heat, as on first exposure or during water restriction, the associated gastrointestinal symptoms (anorexia, nausea, vomiting) may so mask or replace the sensation of thirst that in spite of considerable water deficits, there is no desire for water and even a distaste for it. Thirst may then fail completely as an index of the water needs.

On the first day in humid heat, the voluntary fluid intake during work falls well below the sweat output and large water deficits accumulate (Chart 13). The resultant dehydration may be a factor in the poor performance on this day. With continued exposure to heat, the voluntary water intake during work increases and more nearly approaches the sweat loss (Chart 13). Smaller water deficits result and performance is aided. It is not clear whether this voluntary increase in water intake is the result of the removal of symptoms masking thirst, an increased sensitivity of the thirst mechanism or merely a learning of the need for water.

Full Water Replacement. Drinking water in amounts equal to the

sweat output improves the work performance of men during their first exposure to humid heat (Chart 14).

On their first two days in humid heat, 4 men (Group A) drank water (every 20 to 30 minutes) in amounts equal to the sweat loss. Their performance was compared with that of 4 comparable men (Group B) who drank water as they desired. The improved performance of the group (A) with water replacement is indicated by the greater number

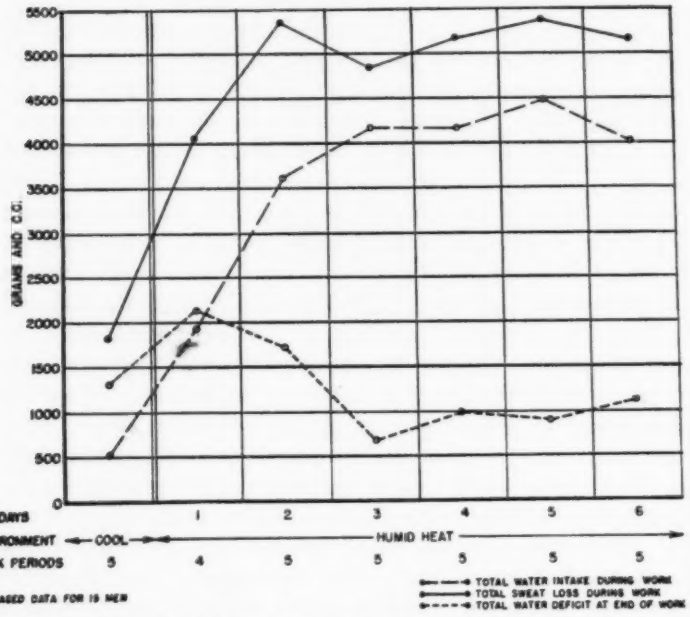

CHART 13. RELATION OF WATER INTAKE TO WEIGHT (SWEAT) LOSS DURING WORK IN HUMID HEAT

of men who completed all of the work periods and by the lower heart rates and rectal temperatures (chart 14). Though improved, this performance was still typically that of unacclimatized men. Postural hypotension with syncope was absent in the forced drinking group but occurred in two men in the "ad lib" group (B). Note the markedly deficient water intake of the "ad lib" group on the first day and the increased intake on the second day.

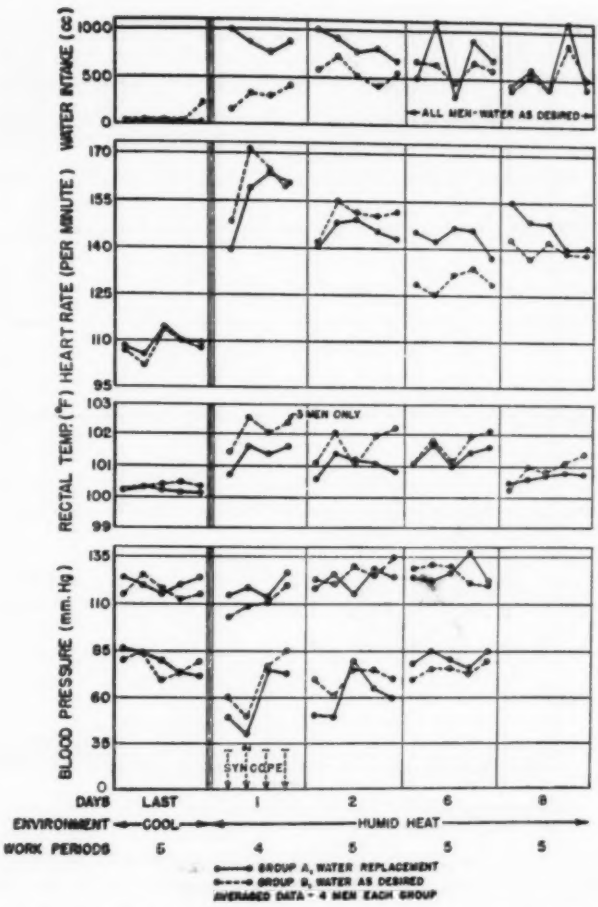

CHART 14. EFFECT OF DRINKING WATER IN AMOUNTS EQUAL TO THE WEIGHT (SWEAT) LOSS ON WORK-PERFORMANCE DURING THE FIRST DAYS IN HUMID HEAT

Sweating and Water Intake. A lay belief persists that the drinking of water promotes sweating and that men may be trained to reduce their water requirements. In this study, sweating was independent

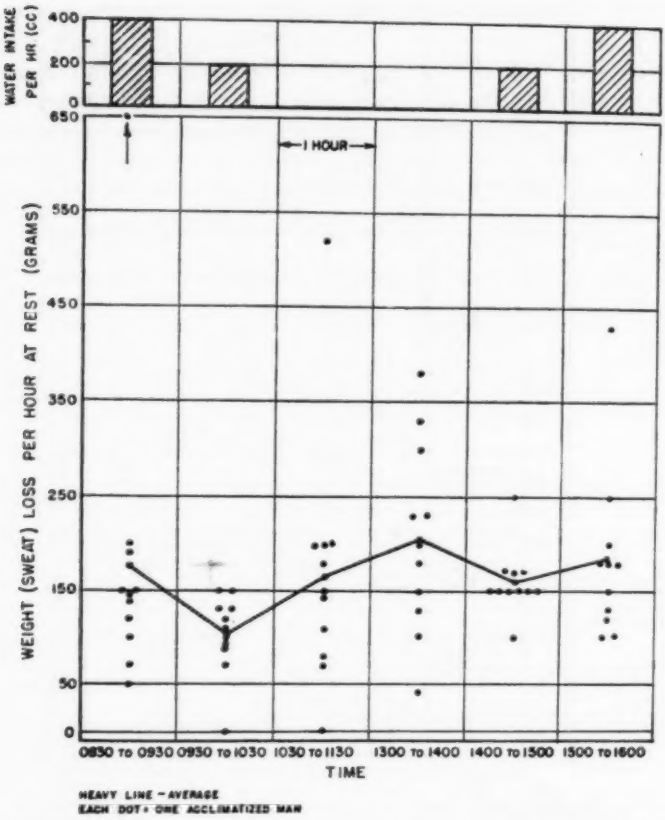

CHART 15. EFFECT OF VARIATIONS IN WATER INTAKE ON THE WEIGHT (SWEAT) LOST BY CLOTHED MEN (ACCLIMATIZED) RESTING IN HUMID HEAT

The subject who lost 650 grams during the first hour is the same man who lost "no weight" during the second and third hours. These three weighings are seriously questioned. His losses during the 4th, 5th, and 6th hours were 300, 250, 180 grams respectively.

of the water intake both for resting (Chart 15) and working (Chart 16) acclimatized men.

The weight (sweat) loss per hour of a group of 11 clothed resting

men was not significantly different whether each man drank 400 cc., 200 cc., or no water during the hour (Chart 15).

The weight (sweat) loss of men working with a restricted water intake was as great as the weight (sweat) loss of the same men working with a water intake sufficient to satisfy their thirst (Chart 16). On one day six (6) acclimatized and stabilized men worked with 150 cc.

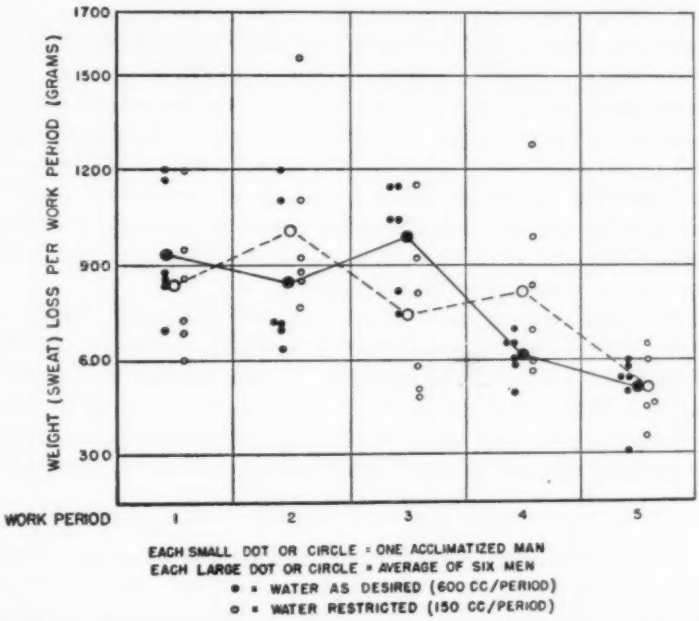

CHART 16. EFFECT OF VARIATIONS IN WATER INTAKE ON THE WEIGHT (SWEAT) LOST BY CLOTHED MEN (ACCLIMATIZED) WORKING IN HUMID HEAT

of water per hour from 6 A.M. to 6 P.M. After 6 P.M. and all of the next day, these men rested and drank water as desired. On the following day, they drank 600 cc. (enough to satisfy thirst) each work period and as much as they desired at all other times. Both the range and the average of the sweat losses for corresponding periods was the same whether water was restricted or not restricted (Chart 16). The reduction in weight (sweat) loss during the afternoon (4th, 5th) work-

periods was an unexplained occurrence in these experiments. Since it occurred to an equal degree whether the water intake was adequate or restricted, it is probably not related to dehydration.

Restriction of Water Intake. Suddenly restricting the water intake of acclimatized working men causes a marked general deterioration, impairs performance and induces physiologic changes similar to those present in unacclimatized men working in humid heat.

Chart 17 contrasts the performance of six acclimatized men when water was given as desired (600 cc./hr) with their performance when water was restricted (150 cc./hr). These are the same men whose sweat losses are indicated in Chart 16. The deteriorated performance when water was restricted is evident in the higher and progressively rising heart rates and rectal temperatures and in the increasing vascular instability. Note the falling systolic blood pressure and the narrowing pulse pressure. During water restriction, one man developed postural hypotension with syncope after the third work period and was unable to work after the fourth period.

The chart does not show other, even more important, changes in these men; the total incapacitation of some, the ineffective working of the others who remain on their feet. It does not show the complete loss of motivation and morale, nor how acclimatized subjects who had performed a given task easily, energetically and cheerfully are reduced to apathetic, listless, plodding men straining to finish the same task.

FACTORS INFLUENCING THE PERFORMANCE OF ACCLIMATIZED MEN

Water Intake and Physical Fitness. The importance of water intake and physical fitness have already been discussed. Of the factors influencing the performance of acclimatized men, adequate water intake is the most important (Chart 17). Then follows physical fitness. In the heat, the fit man is superior to his unfit colleague by approximately the same margin as in the cool environment (Chart 4).

Clothing. Men worked in humid heat with greatest comfort, lowest heart rates, rectal temperatures and sweat losses when they wore only cotton shorts, socks and shoes. Additional clothing increased the discomfort and the physiologic disturbances. Chart 18 (first half), indicates the improved performance during each work period when coveralls were discarded and shorts alone were worn. Wet clothing

imposed less stress than dry clothing. Chart 18 (second half) indicates the definite, though small, improvement when 8 men worked in wet coveralls. In this experiment, half of the men received a dry coverall

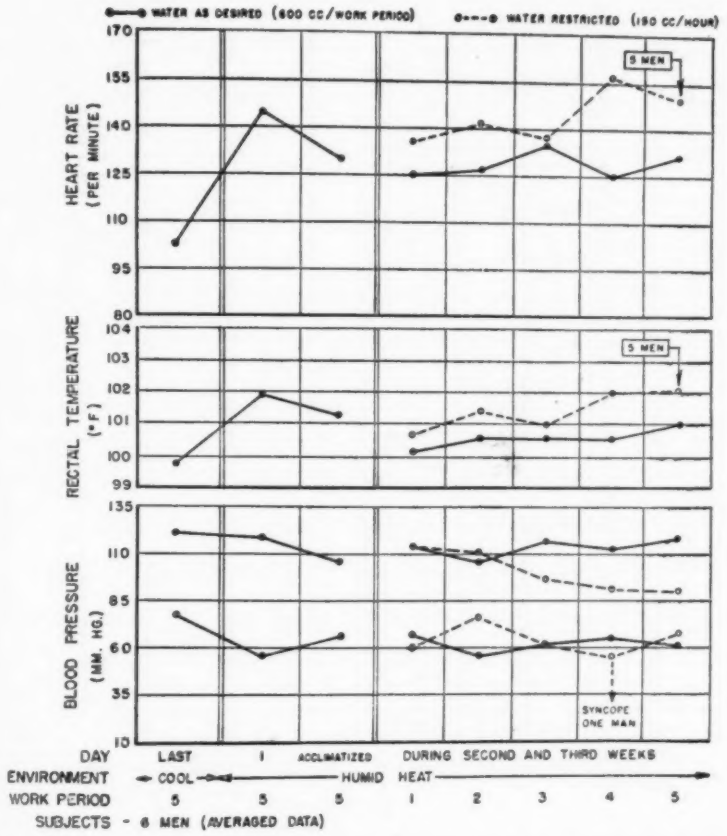

CHART 17. EFFECT OF RESTRICTION OF WATER INTAKE ON THE PERFORMANCE OF ACCLIMATIZED MEN WORKING IN HUMID HEAT

at the beginning of each work period, the other half of the men a wet coverall. On the next day the clothing was reversed so that each man wore wet garments for one day, dry garments the other day.

Rest at Night. Adequate rest at night is necessary for good performance in humid heat. Deprived of sleep, even acclimatized men

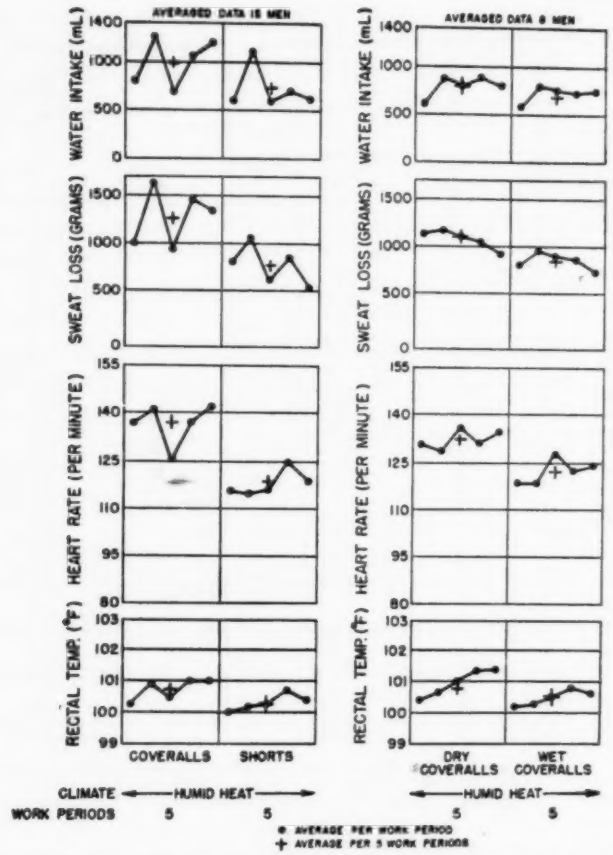

CHART 18. EFFECT OF CLOTHING ON THE PERFORMANCE OF ACCLIMATIZED MEN WORKING IN HUMID HEAT

work ineffectively and inefficiently the next day. The loss of sleep and adequate rest appears to be a more serious handicap at high temperatures than in temperate environments.

Alcohol. The "hangover" of alcoholic intoxication impairs work performance the next day.

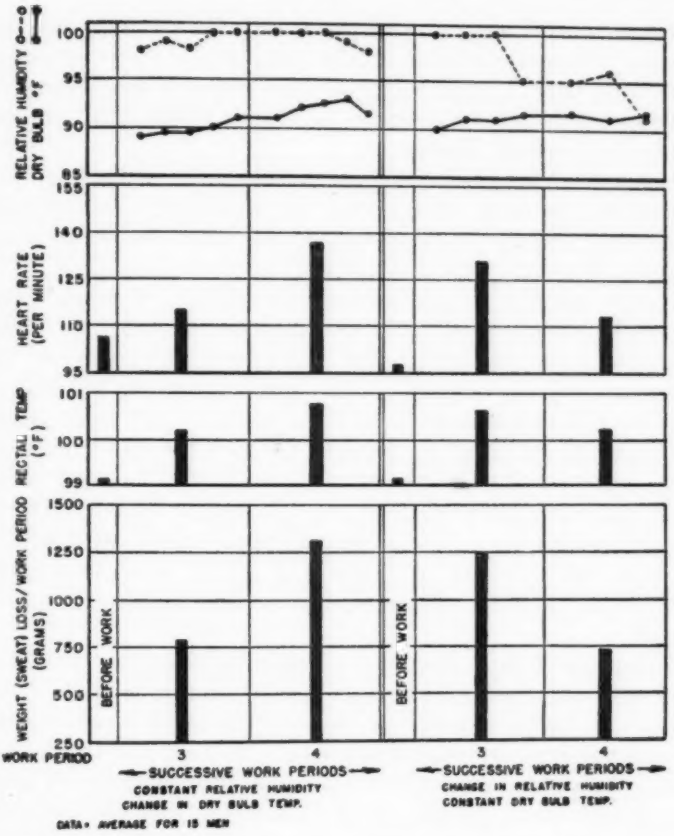

CHART 19. EFFECT OF RELATIVELY SMALL CHANGES IN ENVIRONMENT ON THE HEART RATE, RECTAL TEMPERATURE, AND WEIGHT (SWEAT) LOSS OF ACCLIMATIZED MEN WORKING IN HUMID HEAT

Within a two hour period, three men drank sufficient whiskey and beer to become rapidly and markedly intoxicated. The next morning these men worked with faster heart rates, higher rectal temperatures

and greater weight (sweat) losses than on the previous day. By afternoon, they had improved and their performance was comparable in all respects to that of the previous day.

Effect of Small Changes in the Environment. For the work performed, the environmental conditions of this study impose severe stresses on human tolerance. Under such conditions relatively small changes in the environment alter performance and induce considerable, and even marked, physiologic changes.

In Chart 19 are plotted the observations on 15 acclimatized men during two successive work periods on two widely separated days. The double, central vertical line divides the chart into the two days. Psychrometric data were obtained at 15 minute intervals.

On the first day, the relative humidity remained "constant" while the dry bulb temperature during the 4th period rose about 2°F. higher than that during the third period. As a result the same work was performed with an increase in heart rate (115/min to 137/min), a higher rectal temperature (100.2°F. to 100.7°F.) and more profuse sweating (785 grams to 1306 grams). On the other day the dry bulb temperature remained "constant" while the relative humidity during the fourth period fell to 91%–95% from a level of 95%–100% during the third work period. The same work was performed with a decrease in heart rate (131/min to 113/min), a fall in rectal temperature (100.6°F. to 100.2°F.) and less profuse sweating (1248 grams to 725 grams).

Although such alterations in the actual environment are small, they represent considerable, and at times marked, changes in the available avenues for the loss of heat from the body. Heat loss depends on the thermal and evaporative gradients between the body and the environment. At high environmental temperatures these gradients are small and therefore their changes, and the changes in heat loss, are great whenever the environment varies, even though slightly.

DISCUSSION

Acclimatization to heat appears to be a complex physiologic readjustment which cannot be defined adequately by the simple measurements made in this study. Therefore, no attempt will be made to discuss or elucidate the mechanisms of acclimatization to heat. It is

rather the purpose of this report to present a series of systematic observations on healthy young men exposed to humid (tropical) heat and to derive from these observations several general principles which govern the acclimatization and performance of men in humid, hot environments. These principles do not differ in their essentials from those already reported (16) for men in dry (desert) heat. It is necessary that men be regulated according to these rules if they are to work efficiently and effectively in humid, or dry, heat and avoid undesirable symptoms and disability. These principles are as applicable to workers in hot industries as to troops engaged in military operations.

Of the factors influencing the performance of men in humid heat, acclimatization is the most important. It is essential to appreciate that on first exposure to hot environments, men are physiologically incapable of working as hard or as long as in temperate environments. Therefore, they should not be expected to do so, and to force them to attempt such work, will result in the disability of many men. The increased thermal load makes even the most physically fit man react temporarily like an "unfit" man. Because of this it is not possible on the basis of performance and of concepts of fitness formulated in cool environments to predict the reactions or the work capacity of men when they first work in humid heat. For the same reason, prolonged and strenuous work in cool environments does not serve to prevent the thermally induced "unfitness" which can be overcome only by training (i.e., working) in the hot environment. The most complete adaptation to work in the heat is attained most quickly when men undertake and continue progressively increasing amounts of work coincidently with the onset of continuous residence in the hot environment. When acclimatized, men work as easily and almost as efficiently in humid heat as in a cool environment. Further studies have indicated that men acclimatized to one hot environment cannot immediately undertake strenuous work in hotter or more humid surroundings, but must be reacclimatized to their new environment.

The performance of acclimatized men in humid heat is influenced by the same factors which affect performance in cool environments. However, due to the ever present stress of the added thermal load, performance is more easily disturbed by those factors which impair work output in any climate. Of these, the lack of physical fitness and

the lack of water and salt are the most important. Added clothing and equipment, lack of sleep, rest and food all reduce the efficiency of performance, but not so disablingly.

Although fit men may be as severely incapacited on first working in the heat as unfit men, men in good physical condition tend to acclimatize more rapidly than unfit men. When acclimatized, the more fit men re-acquire their superior performance and work more efficiently and have a greater work output than unfit men. Since acclimatization is quickly attained (one to two weeks at most), men in good physical condition are in the long run the best men for work in hot environments.

In humid heat, sweating is in excess of purposeful needs. In the environment of this study only one-third of the secreted sweat was evaporated and cooled the body, the remainder ran off and constituted an utter waste of water and salt. Nevertheless, sweat continues to be secreted in profuse and excess quantities as long as work is continued. Furthermore, its flow is not materially reduced as the body water decreases and moderate dehydration approaches. In this study, the water and salt losses of the sweat equalled those of men working in a hot dry (simulated desert) environment (16). These losses must be replaced. Failure to do so leads quickly to a deterioration of performance which rapidly progresses to marked inefficiency or total disability, even in the most fit and fully acclimatized men. This deterioration is striking, at times alarming. It is remedied completely by restoring the water and salt balance.

Whenever men live and work for long periods in hot environments, the question of deterioration of performance arises. White men transplanted to the tropics have shown such changes (2, 3, 4). An attempt to produce physiologic deterioration of performance experimentally yielded equivocal results. In one experiment, four men working in the humid heat during a continuous stay of 23 days developed a definite deterioration of performance. This was characterized by higher heart rates and rectal temperatures, more fatigue and discomfort during a standard piece of work than at the peak of acclimatization. After 23 days, the men were removed into the out-of-doors for four days after which they returned to the heat. They now performed the standard work as efficiently and easily as at the peak of acclimatization. An

attempt to achieve a similar deterioration in 15 men who worked in the humid heat during a stay of 28 consecutive days resulted in failure. This leaves for further study the question of the experimental production of deterioration in simulated tropical heat.

SUMMARY

Men adapt themselves to work in humid heat by a process of acclimatization which enables them to work more efficiently and with less risk of illness than when first exposed. The acclimatized man works with a lower heart rate, lower skin and rectal temperature, more stable blood pressure and less discomfort than when unacclimatized. Acclimatization to heat begins with the first exposure, is achieved most rapidly and completely by progressively increased work in the heat, and is complete in 7 to 10 days. Resting in humid heat induces but little acclimatization. Physically fit men acclimatize more rapidly than unfit men and when acclimatized are capable of more efficient work. Acclimatization develops most rapidly when the original environment is warm (summer) and is retained longest when the return is into a warm climate. Strenuous work on first exposure to humid heat is not well tolerated and leads to disability which, however, need not retard nor decrease the final acclimatization attained, *provided* rest, water and salt are supplied. There is a measure of cross acclimatization between hot-dry and hot-humid environments.

The performance of acclimatized men in humid heat is impaired most seriously by lack of adequate water intake and lack of physical fitness. It is also affected adversely, but not so severely, by lack of rest and sleep, by added clothing and equipment, alcohol and long periods of work.

Sweating in humid heat is profuse, grossly inefficient, wastes water and salt and is independent of the fluid intake. Replacement of the lost water and salt is essential to efficient performance. Thirst is a lagging guide to these needs.

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BOOK REVIEWS

(These reviews represent the individual opinions of the reviewers and not necessarily those of the members of the Editorial Board of this Journal.)

Hypertension and Hypertensive Disease. By W. GOLDRING and H. CHASSIS. 253 pp. Illus. $3.50. The Commonwealth Fund, New York, 1944.

This volume presents the clinical and physiological observations of the authors during fifteen years' study of hypertensive patients. The book deals with three different types of material: in Chapters I, II, and VIII hypertension is defined and the clinical aspects and management of hypertensive disease are described. While brief, they are clearly and concisely written, and offer an excellent summary of the present day concept of clinical hypertension.

The body of the book is devoted to the authors' investigations of the hemodynamics of the general circulation and of the kidney in hypertension, together with their interpretation of the results. Detailed descriptions of the methods used are given in the Appendix. These are among the most extensive studies ever made of the pathological physiology of hypertension, and they deserve the thoughtful attention of every student in this field.

The remainder of the book is an evaluation of the rôle of a primary renal mechanism in the genesis of hypertension, and of thiocyanate therapy, sympathectomy and unilateral nephrectomy in its treatment. Here a great deal of controversial material is presented, not always in its most convincing light. For instance, it is unfortunate that the authors did not publish the blood thiocyanate concentrations attained in their patients. While they state that their method of attempting to control thiocyanate dosage by calculating the residual drug in the body is "more satisfactory than blood concentration," the high daily dosages recorded in the early days of treatment and the exceedingly high incidence of toxic symptoms induced, including two deaths, leads one to question the statement. Likewise, their remarks on sympathectomy, based on their own small series of five cases, are of limited value from the standpoint of adequately comprehending the status of sympathectomy as a whole. The authors conclude that experimentally induced renal hypertension in animals is fundamentally different in genesis from that occurring spontaneously in man. The origin of essential hypertension is still unknown.

C. B. T.

BOOKS RECEIVED FOR REVIEW

An Introduction to Pharmacology and Therapeutics. By J. A. GUNN. 259 pp. $2.25. Oxford University Press London: Humphrey Milford, 1944.

Atlas of the Blood in Children. By KENNETH D. BLACKFAN and LOUIS K. DIAMOND. 320 pp. $12.00. The Commonwealth Fund 1944, New York.

Escleroses Valvulares Calcificadas. By Dr. ROBERTO MENEZES DE OLIVEIRA. 154 pp.

Gynecological and Obstetrical Urology. By HOUSTON S. EVERETT. Illus. 503 pp. $6.00. The Williams & Wilkins Company, Baltimore, 1944.

Ourselves Unborn. By GEORGE W. CORNER. Illus. 180 pp. $3.00. Yale University Press, New Haven, 1944.

Modern Clinical Syphilology. By JOHN H. STOKES. [1372 pp. $10.00. W. B. Saunders Company, 1944. Philadelphia, London.

The Precentral Motor Cortex. By PAUL C. BUCY. 605 pp. $4.50. University of Illinois Press, Urbana, Illinois.